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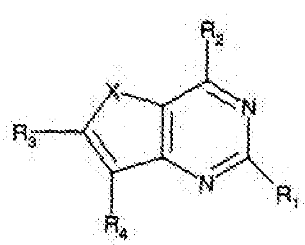

(1)

(57) Abstract: A compound of formula (I), wherein X is S or O; R_1 is selected from H, alkyl, aryl, hydroxy, alkoxy, aryloxy, thioalkyl, thioaryl, halogen, CN, COR_5, CO_2R_5, $CONR_6R_7$, $CONR_5NR_6R_7$, NR_6R_7, $NR_5CONR_6R_7$, NR_5COR_6, $NR_5CO_2R_8$, and $NR_5SO_2R_8$; R_2 is selected from aryl attached via an unsaturated carbon atom; R_3 is selected from H, alkyl, hydroxy, alkoxy, halogen, CN and NO_2; R_4 is selected from H, alkyl, aryl, hydroxy, alkoxy, aryloxy, thioalkyl, thioaryl, halogen, CN, NO_2, COR_5, CO_2R_5, $CONR_6R_7$, $CONR_5NR_6R_7$, NR_6R_7, $NR_5CONR_6R_7$, NR_5COR_6, $NR_5CO_2R_8$ and $NR_5SO_2R_8$; R_5, R_6 and R_7 are independently selected from H, alkyl and aryl or where R_6 and R_7 are in an (NR_6R_7) group, R_6 and R_7 may be linked to form a heterocyclic group, or where R_5, R_6 and R_7 are in a $(CONR_5NR_6R_7)$ group, R_5 and R_6 may be linked to form a heterocyclic group; and R_8 is selected from alkyl and aryl, or a pharmaceutically acceptable salt thereof or prodrug thereof, and the use thereof in therapy and in the treatment or prevention of a disorder in which the blocking of purine receptors, particularly adenosine receptors and more particularly A_{2A} receptors, may be beneficial, particularly wherein said disorder is a movement disorder such a Parkinson's disease or said disorder is depression, cognitive or memory impairment, acute or chronic pain, ADHD or narcolepsy, or wherein said medicament is for neuroprotection in a subject.

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THIENO(3,2-d)PYRIMIDINES AND FURANO(3,2-d)PYRIMIDINES AND THEIR USE AS PURINERGIC RECEPTOR ANTAGONISTS

The present invention relates to thieno(3,2-d)pyrimidines and furano(3,2-d)pyrimidines and their use in therapy. In particular, the present invention relates to the treatment of disorders in which the reduction of purinergic neurotransmission could be beneficial. The invention relates in particular to blockade of adenosine receptors and particularly adenosine A_{2A} receptors, and to the treatment of movement disorders such as Parkinson's disease.

Movement disorders constitute a serious health problem, especially amongst the elderly sector of the population. These movement disorders are often the result of brain lesions. Disorders involving the basal ganglia which result in movement disorders include Parkinson's disease, Huntington's chorea and Wilson's disease. Furthermore, dyskinesias often arise as sequelae of cerebral ischaemia and other neurological disorders.

There are four classic symptoms of Parkinson's disease: tremor, rigidity, akinesia and postural changes. The disease is also commonly associated with depression, dementia and overall cognitive decline. Parkinson's disease has a prevalence of 1 per 1,000 of the total population. The incidence increases to 1 per 100 for those aged over 60 years. Degeneration of dopaminergic neurones in the substantia nigra and the subsequent reductions in interstitial concentrations of dopamine in the striatum are critical to the development of Parkinson's disease. Some 80% of cells from the substantia nigra need to be destroyed before the clinical symptoms of Parkinson's disease are manifested.

Current strategies for the treatment of Parkinson's disease are based on transmitter replacement therapy (L-dihydroxyphenylacetic acid (L-DOPA)), inhibition of monoamine oxidase (e.g. Deprenyl®), dopamine receptor agonists (e.g. bromocriptine and apomorphine) and anticholinergics (e.g. benztrophine, orphenadrine). Transmitter replacement therapy in particular does not provide consistent clinical benefit, especially after prolonged treatment when "on-off" symptoms develop, and this treatment has also been associated with involuntary movements of athetosis and chorea, nausea and vomiting. Additionally current therapies do not treat the underlying neurodegenerative disorder resulting in a continuing cognitive decline in patients. Despite new drug approvals, there is

still a medical need in terms of improved therapies for movement disorders, especially Parkinson's disease. In particular, effective treatments requiring less frequent dosing, effective treatments which are associated with less severe side-effects, and effective treatments which control or reverse the underlying neurodegenerative disorder, are required.

Blockade of A_2 adenosine receptors has recently been implicated in the treatment of movement disorders such as Parkinson's disease (Richardson, P.J. *et al.*, *Trends Pharmacol. Sci.* 1997, 18, 338-344) and in the treatment of cerebral ischaemia (Gao, Y. and Phillis, J.W., *Life Sci.* 1994, 55, 61-65). The potential utility of adenosine A_{2A} receptor antagonists in the treatment of movement disorders such as Parkinson's Disease has recently been reviewed (Mally, J. and Stone, T.W., *CNS Drugs*, 1998, 10, 311-320).

Adenosine is a naturally occurring purine nucleoside which has a wide variety of well-documented regulatory functions and physiological effects. The central nervous system (CNS) effects of this endogenous nucleoside have attracted particular attention in drug discovery, owing to the therapeutic potential of purinergic agents in CNS disorders (Jacobson, K.A. *et al.*, *J. Med. Chem.* 1992, 35, 407-422). This therapeutic potential has resulted in considerable recent research endeavour within the field of adenosine receptor agonists and antagonists (Bhagwhat, S.S.; Williams, M. *Exp. Opin. Ther. Patents* 1995, 5,547-558).

Adenosine receptors represent a subclass (P_1) of the group of purine nucleotide and nucleoside receptors known as purinoreceptors. The main pharmacologically distinct adenosine receptor subtypes are known as A_1, A_{2A}, A_{2B} (of high and low affinity) and A_3 (Fredholm, B.B., *et al.*, *Pharmacol. Rev.* 1994, 46, 143-156). The adenosine receptors are present in the CNS (Fredholm, B.B., *News Physiol. Sci.*, 1995, 10, 122-128).

The design of P_1 receptor-mediated agents has been reviewed (Jacobson, K.A., Suzuki, F., *Drug Dev. Res.*, 1997, 39, 289-300; Baraldi, P.G. *et al.*, *Curr. Med. Chem.* 1995, 2, 707-722), and such compounds are claimed to be useful in the treatment of cerebral ischemia or neurodegenerative disorders, such as Parkinson's disease (Williams, M. and Burnstock, G.

Purinergic Approaches Exp. Ther. (1997), 3-26. Editor: Jacobson, Kenneth A.; Jarvis, Michael F. Publisher: Wiley-Liss, New York, N.Y.)

It has been speculated that xanthine derivatives such as caffeine may offer a form of treatment for attention-deficit hyperactivity disorder (ADHD). A number of studies have demonstrated a beneficial effect of caffeine on controlling the symptoms of ADHD (Garfinkel, B.D. *et al.*, *Psychiatry*, 1981, **26**, 395-401). Antagonism of adenosine receptors is thought to account for the majority of the behavioural effects of caffeine in humans and thus blockade of adenosine A_{2A} receptors may account for the observed effects of caffeine in ADHD patients. Therefore a selective A_{2A} receptor antagonist may provide an effective treatment for ADHD but without the unwanted side-effects associated with current therapy.

Adenosine receptors have been recognised to play an important role in regulation of sleep patterns, and indeed adenosine antagonists such as caffeine exert potent stimulant effects and can be used to prolong wakefulness (Porkka-Heiskanen, T. *et al.*, *Science*, 1997, **276**, 1265-1268). Recent evidence suggests that a substantial part of the actions of adenosine in regulating sleep is mediated through the adenosine A_{2A} receptor (Satoh, S., *et al.*, *Proc. Natl. Acad. Sci.*, USA, 1996). Thus, a selective A_{2A} receptor antagonist may be of benefit in counteracting excessive sleepiness in sleep disorders such as hypersomnia or narcolepsy.

It has recently been observed that patients with major depression demonstrate a blunted response to adenosine agonist-induced stimulation in platelets, suggesting that a dysregulation of A_{2A} receptor function may occur during depression (Berk, M. et al, 2001, *Eur. Neuropsychopharmacol.* 11, 183-186). Experimental evidence in animal models has shown that blockade of A_{2A} receptor function confers antidepressant activity (El Yacoubi, M et al. *Br. J. Pharmacol.* 2001, 134, 68-77). Thus, A_{2A} receptor antagonists may offer a novel therapy for the treatment of major depression and other affective disorders in patients.

The pharmacology of adenosine A_{2A} receptors has been reviewed (Ongini, E.; Fredholm, B.B. *Trends Pharmacol. Sci.* 1996, 17(10), 364-372). One potential underlying mechanism in the aforementioned treatment of movement disorders by the blockade of A_2 adenosine receptors is the evidence of a functional link between adenosine A_{2A} receptors to dopamine

D_2 receptors in the CNS. Some of the early studies (e.g. Ferre, S. *et al.*, Stimulation of high-affinity adenosine A_2 receptors decreases the affinity of dopamine D_2 receptors in rat striatal membranes. *Proc. Natl. Acad. Sci.* U.S.A. 1991, 88, 7238-41) have been summarised in two more recent articles (Fuxe, K. *et al.*, *Adenosine Adenine Nucleotides Mol. Biol. Integr. Physiol.*, [Proc. Int. Symp.], 5th (1995), 499-507. Editors: Belardinelli, Luiz; Pelleg, Amir. Publisher: Kluwer, Boston, Mass.; Ferre, S. *et al.*, *Trends Neurosci.* 1997, 20, 482-487).

As a result of these investigations into the functional role of adenosine A_{2A} receptors in the CNS, especially *in vivo* studies linking A_2 receptors with catalepsy (Ferre *et al.*, *Neurosci. Lett.* 1991, 130, 162-4; Mandhane, S.N. *et al.*, *Eur. J. Pharmacol.* 1997, 328, 135-141) investigations have been made into agents which selectively bind to adenosine A_{2A} receptors as potentially effective treatments for Parkinson's disease.

While many of the potential drugs for treatment of Parkinson's disease have shown benefit in the treatment of movement disorders, an advantage of adenosine A_{2A} antagonist therapy is that the underlying neurodegenerative disorder may also be treated. The neuroprotective effect of adenosine A_{2A} antagonists has been reviewed (Ongini, E.; Adami, M.; Ferri, C.; Bertorelli, R., *Ann. N. Y. Acad. Sci.* 1997, 825(Neuroprotective Agents), 30-48). In particular, compelling recent evidence suggests that blockade of A_{2A} receptor function confers neuroprotection against MPTP-induced neurotoxicity in mice (Chen, J-F., *J. Neurosci.* 2001, 21, RC143). In addition, several recent studies have shown that consumption of dietary caffeine, a known adenosine A_{2A} receptor antagonist, is associated with a reduced risk of Parkinson's disease in man (Ascherio, A. et al, *Ann Neurol.*, 2001, 50, 56-63; Ross G W, et al., *JAMA*, 2000, 283, 2674-9). Thus, A_{2A} receptor antagonists may offer a novel treatment for conferring neuroprotection in neurodegenerative diseases such as Parkinson's disease.

Xanthine derivatives have been disclosed as adenosine A_2 receptor antagonists as useful for treating various diseases caused by hyperfunctioning of adenosine A_2 receptors, such as Parkinson's disease (see, for example, EP-A-565377).

One prominent xanthine-derived adenosine A_{2A} selective antagonist is CSC [8-(3-chlorostyryl)caffeine] (Jacobson *et al.*, *FEBS Lett.*, 1993, 323, 141-144).

Theophylline (1,3-dimethylxanthine), a bronchodilator drug which is a mixed antagonist at adenosine A_1 and A_{2A} receptors, has been studied clinically. To determine whether a formulation of this adenosine receptor antagonist would be of value in Parkinson's disease an open trial was conducted on 15 Parkinsonian patients, treated for up to 12 weeks with a slow release oral theophylline preparation (150 mg/day), yielding serum theophylline levels of 4.44 mg/L after one week. The patients exhibited significant improvements in mean objective disability scores and 11 reported moderate or marked subjective improvement (Mally, J., Stone, T.W. *J. Pharm. Pharmacol.* 1994, 46, 515-517).

KF 17837 [(E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine] is a selective adenosine A_{2A} receptor antagonist which on oral administration significantly ameliorated the cataleptic responses induced by intracerebroventricular administration of an adenosine A_{2A} receptor agonist, CGS 21680. KF 17837 also reduced the catalepsy induced by haloperidol and reserpine. Moreover, KF 17837 potentiated the anticataleptic effects of a subthreshold dose of L-DOPA plus benserazide, suggesting that KF 17837 is a centrally active adenosine A_{2A} receptor antagonist and that the dopaminergic function of the nigrostriatal pathway is potentiated by adenosine A_{2A} receptor antagonists (Kanda, T. *et al.*, *Eur. J. Pharmacol.* 1994, 256, 263-268). The structure activity relationship (SAR) of KF 17837 has been published (Shimada, J. *et al.*, *Bioorg. Med. Chem. Lett.* 1997, 7, 2349-2352). Recent data has also been provided on the A_{2A} receptor antagonist KW-6002 (Kuwana, Y *et al.*, *Soc. Neurosci. Abstr.* 1997, 23, 119.14; and Kanda, T. *et al.*, *Ann. Neurol.* 1998, 43(4), 507-513).

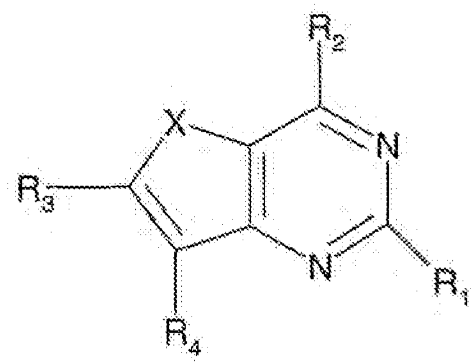
New non-xanthine structures sharing these pharmacological properties include SCH 58261 and its derivatives (Baraldi, P.G. *et al.*, Pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine Derivatives: Potent and Selective A_{2A} Adenosine Antagonists. *J. Med. Chem.* 1996, 39, 1164-71). SCH 58261 (7-(2-phenylethyl)-5-amino-2-(2-furyl)-pyrazolo-[4,3-e]-1,2,4-triazolo[1,5-c] pyrimidine) is reported as effective in the treatment of movement disorders (Ongini, E. *Drug Dev. Res.* 1997, 42(2), 63-70) and has been followed up by a later series of compounds (Baraldi, P.G. *et al.*, *J. Med. Chem.* 1998, 41(12), 2126-2133).

The foregoing discussion indicates that a potentially effective treatment for movement disorders in humans would comprise agents which act as antagonists at adenosine A_{2A} receptors.

It has now been found that thieno(3,2-d)pyrimidines and furano(3,2-d)pyrimidines, which are structurally unrelated to known adenosine receptor antagonists, exhibit unexpected antagonist binding affinity at adenosine (P_1) receptors, and in particular at the adenosine A_{2A} receptor. Such compounds may therefore be useful for the treatment of disorders in which the blocking of purine receptors, particularly adenosine receptors and more particularly adenosine A_{2A} receptors, may be beneficial. In particular such compounds may be suitable for the treatment of movement disorders, such as disorders of the basal ganglia which result in dyskinesias. Disorders of particular interest include Parkinson's disease, Alzheimer's disease, spasticity, Huntington's chorea and Wilson's disease.

Such compounds may also be particularly suitable for the treatment of depression, cognitive or memory impairment including Alzheimer's disease, acute or chronic pain, ADHD, narcolepsy or for neuroprotection.

According to the present invention there is provided a compound of formula (I):



(I)

wherein

X is S or O;

R_1 is selected from H, alkyl, aryl, hydroxy, alkoxy, aryloxy, thioalkyl, thioaryl, halogen, CN, COR_5, CO_2R_5, $CONR_6R_7$, $CONR_5NR_6R_7$, NR_6R_7, $NR_5CONR_6R_7$, NR_5COR_6, $NR_5CO_2R_8$, and $NR_5SO_2R_8$;

R_2 is selected from aryl attached via an unsaturated carbon atom;

R_3 is selected from H, alkyl, hydroxy, alkoxy, halogen, CN and NO_2;

R_4 is selected from H, alkyl, aryl, hydroxy, alkoxy, aryloxy, thioalkyl, thioaryl, halogen, CN, NO_2, COR_5, CO_2R_5, $CONR_6R_7$, $CONR_5NR_6R_7$, NR_6R_7, $NR_5CONR_6R_7$, NR_5COR_6, $NR_5CO_2R_8$ and $NR_5SO_2R_8$;

R_5, R_6 and R_7 are independently selected from H, alkyl and aryl, or where R_6 and R_7 are in an (NR_6R_7) group, R_6 and R_7 may be linked to form a heterocyclic group, or where R_5, R_6 and R_7 are in a $(CONR_5NR_6R_7)$ group, R_5 and R_6 may be linked to form a heterocyclic group; and

R_8 is selected from alkyl and aryl,

or a pharmaceutically acceptable salt thereof or prodrug thereof.

As used herein, the term "alkyl" means a branched or unbranched, cyclic or acyclic, saturated or unsaturated (e.g. alkenyl or alkynyl) hydrocarbyl radical which may be substituted or unsubstituted. Where cyclic, the alkyl group is preferably C_3 to C_{12}, more preferably C_5 to C_{10}, more preferably C_5, C_6 or C_7. Where acyclic, the alkyl group is preferably C_1 to C_{10}, more preferably C_1 to C_6, more preferably methyl, ethyl, propyl (n-propyl or isopropyl), butyl (n-butyl, isobutyl or tertiary-butyl) or pentyl (including n-pentyl and iso-pentyl), more preferably

methyl. It will be appreciated therefore that the term "alkyl" as used herein includes alkyl (branched or unbranched), alkenyl (branched or unbranched), alkynyl (branched or unbranched), cycloalkyl, cycloalkenyl and cycloalkynyl.

As used herein, the term "lower alkyl" means methyl, ethyl, propyl (n-propyl or isopropyl) or butyl (n-butyl, isobutyl or tertiary-butyl).

As used herein, the term "aryl" means an aromatic group, such as phenyl or naphthyl (preferably phenyl), or a heteroaromatic group containing one or more heteroatom(s) preferably selected from N, O and S, such as pyridyl, pyrrolyl, quinolinyl, furanyl, thienyl, oxadiazolyl, thiadiazolyl, thiazolyl, oxazolyl, isoxazolyl, pyrazolyl, triazolyl, imidazolyl or pyrimidinyl.

As used herein, the term "heteroaryl" means an aromatic group containing one or more heteroatom(s) preferably selected from N, O and S, such as pyridyl, pyrrolyl, quinolinyl, furanyl, thienyl, oxadiazolyl, thiadiazolyl, thiazolyl, oxazolyl, isoxazolyl, pyrazolyl, triazolyl, imidazolyl or pyrimidinyl.

As used herein, the term "alkoxy" means alkyl-O-. As used herein, the term "aryloxy" means aryl-O-.

As used herein, the term "halogen" means a fluorine, chlorine, bromine or iodine radical.

As used herein, the term "ortho,ortho-disubstituted aryl groups" refers to aryl groups which are substituted in both ortho positions of the aryl group relative to the point of attachment of the aryl group to the pyrimidine ring.

As used herein, the term "prodrug" means any pharmaceutically acceptable prodrug of a compound of the present invention.

Where any of R_1 to R_{13} is selected from alkyl, alkoxy and thioalkyl, in accordance with formula (I) as defined above, then that alkyl group, or the alkyl group of the alkoxy or thioalkyl group, may be substituted or unsubstituted. Where any of R_1 to R_{13} are selected

from aryl, aryloxy and thioaryl, in accordance with formula (I) as defined above, then said aryl group, or the aryl group of the aryloxy or thioaryl group, may be substituted or unsubstituted. Where R_5 and R_6, or R_6 and R_7, or R_{12} and R_{13}, or R_5 and R_{12} are linked to form a heterocyclic group, the heterocyclic group may be substituted or unsubstituted. Where substituted, there will generally be 1 to 3 substituents present, preferably 1 substituent. Substituents may include:

carbon-containing groups such as

alkyl,	
aryl,	(e.g. substituted and unsubstituted phenyl (including alkylphenyl, alkoxyphenyl and halophenyl),
arylalkyl;	(e.g. substituted and unsubstituted benzyl);

halogen atoms and halogen containing groups such as

haloalkyl	(e.g. trifluoromethyl),
haloaryl	(e.g. chlorophenyl);

oxygen containing groups such as

alcohols	(e.g. hydroxy, hydroxyalkyl, hydroxyaryl, (aryl)(hydroxy)alkyl),
ethers	(e.g. alkoxy, aryloxy, alkoxyalkyl, aryloxyalkyl, alkoxyaryl, aryloxyaryl),
aldehydes	(e.g. carboxaldehyde),
ketones	(e.g. alkylcarbonyl, arylcarbonyl, alkylcarbonylalkyl, alkylcarbonylaryl, arylcarbonylalkyl, arylcarbonylaryl, arylalkylcarbonyl, arylalkylcarbonylalkyl, arylalkylcarbonylaryl)
acids	(e.g. carboxy, carboxyalkyl, carboxyaryl),

acid derivatives such as esters

(e.g. alkoxycarbonyl, aryloxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, alkylcarbonyloxy, alkylcarbonyloxyalkyl),

amides

(e.g. aminocarbonyl, mono- or di-alkylaminocarbonyl, cyclicaminocarbonyl, aminocarbonylalkyl, mono- or di-

alkylaminocarbonylalkyl, arylaminocarbonyl or arylalkylaminocarbonyl, alkylcarbonylamino, arylcarbonylamino or arylalkylcarbonylamino),

carbamates

(eg. alkoxycarbonylamino, aryloxycarbonylamino, arylalkyloxycarbonylamino, aminocarbonyloxy, mono- or di-alkylaminocarbonyloxy, arylaminocarbonyloxy or arylalkylaminocarbonyloxy)

and ureas

(eg. mono- or di-alkylaminocarbonylamino, arylaminocarbonylamino or arylalkylaminocarbonylamino);

nitrogen containing groups such as

amines (e.g. amino, mono- or dialkylamino, cyclicamino, arylamino, aminoalkyl, mono- or dialkylaminoalkyl),

azides,

nitriles (e.g. cyano, cyanoalkyl),

nitro,

sulfonamides (e.g. aminosulfonyl, mono- or di-alkylaminosulfonyl, mono- or di-arylaminosulfonyl, alkyl- or aryl-sulfonylamino, alkyl- or aryl-sulfonyl(alkyl)amino, alkyl- or aryl-sulfonyl(aryl)amino);

sulfur containing groups such as

thiols, thioethers, sulfoxides, and sulfones

(e.g. alkylthio, alkylsulfinyl, alkylsulfonyl, alkylthioalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, arylthio, arylsulfinyl, arylsulfonyl, arylthioalkyl, arylsulfinylalkyl, arylsulfonylalkyl);

heterocyclic groups containing one or more, preferably one, heteroatom,

(e.g. thienyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, oxadiazolyl, thiadiazolyl, aziridinyl, azetidinyl, pyrrolidinyl, pyrrolinyl, imidazolidinyl, imidazolinyl,

pyrazolidinyl, tetrahydrofuranyl, pyranyl, pyronyl, pyridyl, pyrazinyl, pyridazinyl, piperidyl, hexahydroazepinyl, piperazinyl, morpholinyl, thianaphthyl, benzofuranyl, isobenzofuranyl, indolyl, oxyindolyl, isoindolyl, indazolyl, indolinyl, 7-azaindolyl, benzopyranyl, coumarinyl, isocoumarinyl, quinolinyl, isoquinolinyl, naphthridinyl, cinnolinyl, quinazolinyl, pyridopyridyl, benzoxazinyl, quinoxalinyl, chromenyl, chromanyl, isochromanyl, phthalazinyl and carbolinyl); and

silicon-containing groups such as

silanes (e.g. trialkylsilyl).

In one embodiment, where any of R_1 to R_{13} is directly substituted by an alkyl substituent group, or by an alkyl-containing substituent group (such as alkoxy, alkoxyalkyl or alkylcarbonylamino for example), then the alkyl moiety of the substituent group directly attached to any of R_1 to R_{13} may be further substituted by the substituent groups hereinbefore described and particularly by halogen, hydroxy, alkoxy, CN, amines (including amino, mono- and di-alkyl amino) and aryl.

In a further embodiment, where any of R_1 to R_{13} is directly substituted by an aryl substitutent group, or by an aryl-containing substituent group (such as aryloxy or arylaminocarbonylamino for example), then the aryl moiety of the substituent group directly attached to any of R_1 to R_{13} may be further substituted by the substituent groups hereinbefore described and particularly by halogen, alkyl (including CF_3), hydroxy, alkoxy, CN, amines (including amino, mono- and di-alkyl amino) and NO_2.

The terms "directly substituted" and "directly attached", as used herein, mean that the substituent group is bound directly to any of R_1 to R_{13} without any intervening divalent atoms or groups.

In the compounds of formula (I), it is preferred that X is S.

In the compounds of formula (I), R_1 is selected from H, alkyl (including branched and unbranched alkyl, substituted and unsubstituted alkyl, and cyclic and acyclic alkyl), aryl (including heteroaryl), hydroxy, alkoxy, aryloxy, thioalkyl, thioaryl, halogen, CN, COR_5, CO_2R_5, $CONR_6R_7$, $CONR_5NR_6R_7$, NR_6R_7 (including NH_2, monoalkyl amino and dialkylamino), $NR_5CONR_6R_7$, NR_5COR_6, $NR_5CO_2R_8$ and $NR_5SO_2R_8$.

It is preferred that R_1 is selected from alkyl, alkoxy, thioalkyl, NR_6R_7 and NR_5COR_6, and preferably from alkyl and NR_6R_7. In one embodiment, R_1 is selected from NH_2.

Where R_1 is selected from alkyl, alkoxy and alkylthio, then said alkyl group or the alkyl group of the alkoxy or alkylthio is preferably selected from C_{1-6} alkyl (including branched and unbranched alkyl, substituted and unsubstituted alkyl, and cyclic and acyclic alkyl), preferably saturated C_{1-6} alkyl, and more preferably lower alkyl. In a preferred embodiment, R_1 is selected from substituted alkyl, particularly haloalkyl (including CF_3) and arylalkyl (including heteroarylalkyl).

In one embodiment, R_1 is selected from $CONR_5NR_6R_7$, $NR_5CONR_6R_7$, NR_5COR_6, $NR_5CO_2R_8$ and $NR_5SO_2R_8$, and R_5 is H or alkyl, and preferably H.

In one embodiment, R_1 is selected from NR_6R_7 wherein R_6 is preferably selected from H and alkyl (preferably H), and R_7 is a substituted alkyl group represented by $(CR_9R_{10})_nR_{11}$, wherein R_9 and R_{10} are independently selected from H, alkyl and aryl (preferably from H and alkyl, and more preferably from H), n is selected from 1 to 6 (preferably from 2 to 4, more preferably 2), and R_{11} is selected from aryl (including heteroaryl), COR_5, CO_2R_5, $CONR_{12}R_{13}$, $CONR_5NR_{12}R_{13}$, $NR_{12}R_{13}$ (including NH_2, monoalkyl amino and dialkylamino), $NR_5CONR_{12}R_{13}$, NR_5COR_{12}, $NR_5CO_2R_8$ and $NR_5SO_2R_8$ (and preferably from aryl (including heteroaryl), $NR_{12}R_{13}$ (including NH_2, monoalkyl amino and dialkylamino), $NR_5CONR_{12}R_{13}$, NR_5COR_{12}, $NR_5CO_2R_8$ and $NR_5SO_2R_8$), wherein R_5 and R_8 are as hereinbefore defined and wherein R_{12} and R_{13} are independently selected from H, alkyl and aryl, or where R_{12} and R_{13} are in an $(NR_{12}R_{13})$ group, R_{12} and R_{13} may be linked to form a heterocyclic group, or where R_5, R_{12} and R_{13} are in a $(CONR_5NR_{12}R_{13})$ group, R_5 and R_{12} may be linked to form a heterocyclic group.

In the compounds of formula (I), R_2 is substituted or unsubstituted aryl (including heteroaryl) attached via an unsaturated carbon atom. Preferably, the aryl group is a 5- or 6- membered monocyclic aryl group.

Preferably, R_2 is a heteroaryl group, and preferably a heteroaryl group which is attached to the pyrimidine ring of formula (I) such that a heteroatom is adjacent to the unsaturated carbon atom attached to said pyrimidine ring. Preferably, R_2 is an N, O or S-containing heteroaryl group. R_2 may contain one or more heteroatom(s) selected from N, O and S.

It is preferred that the aryl (including heteroaryl) group of R_2 is not ortho,ortho-disubstituted. Preferably, the aryl (including heteroaryl) group of R_2 is not substituted at either ortho position. As used herein, reference to ortho-substitution of the R_2 group means the ortho positions of the R_2 group relative to the point of attachment of R_2 to the pyrimidine moiety of formula (I).

In a preferred embodiment, R_2 is selected from furyl (including 2-furyl), thienyl (including 2-thienyl), pyridyl (including 2-pyridyl), thiazolyl (including 2- and 5- thiazolyl), pyrazolyl (including 3-pyrazolyl), triazolyl (including 4-triazolyl), pyrrolyl (including 2-pyrrolyl) and oxazolyl (including 5-oxazolyl). In a further embodiment, R_2 is selected from 2-furyl, 2-thienyl, 2-thiazolyl, 2-pyridyl, 3-pyrazolyl, 2-pyrrolyl, 4-triazolyl and 5-oxazolyl. In a preferred embodiment, R_2 is selected from furyl, thienyl, pyridyl and thiazolyl, and preferably from 2-furyl, 2-thienyl, 2-thiazolyl and 2-pyridyl.

In a particularly preferred embodiment, R_2 is selected from 2-thiazolyl, optionally substituted, particularly by methyl.

In the compounds of formula (I), R_3 is selected from H, alkyl (including haloalkyl (particularly CF_3)), hydroxy, alkoxy (including OCF_3), halogen, CN and NO_2. Preferably, R_3 is selected from H, CF_3, hydroxy, alkoxy, halogen, CN and NO_2, and preferably R_3 is H.

In the embodiment where R_3 is selected from alkyl or alkoxy, then said alkyl group or the alkyl group of said alkoxy is preferably C_{1-6} alkyl (including branched and unbranched alkyl, substituted and unsubstituted alkyl, and cyclic and acyclic alkyl), preferably saturated C_{1-6}

alkyl, and more preferably lower alkyl. In a preferred embodiment of compounds wherein R_5 is selected from alkyl, R_3 is haloalkyl (particularly CF_3).

In the compounds of formula (I), R_4 is selected from H, alkyl (including branched and unbranched alkyl, substituted and unsubstituted alkyl, and cyclic and acyclic alkyl), aryl (including heteroaryl), hydroxy, alkoxy, aryloxy, thioalkyl, thioaryl, halogen, CN, NO_2, COR_5, CO_2R_5, $CONR_6R_7$, $CONR_5NR_6R_7$, NR_6R_7 (including NH_2), $NR_5CONR_6R_7$, NR_5COR_6, $NR_5CO_2R_8$ and $NR_5SO_2R_8$.

Where R_4 is selected from alkyl, preferably R_4 is C_{1-8} alkyl (including branched and unbranched alkyl, substituted and unsubstituted alkyl, and cyclic and acyclic alkyl), preferably saturated C_{1-6} alkyl, and more preferably lower alkyl. In one embodiment, R_4 is selected from substituted alkyl, wherein the substituent groups are selected from halogen, susbtituted and unsubstituted aryl (including heteroaryl), cycloalkyl, non-aromatic heterocyclyl, CO_2R_5, $CONR_6R_7$, $CONR_5NR_6R_7$ and $C(=NR_5)NR_6R_7$, preferably aryl (including heteroaryl) and $CONR_6R_7$, more preferably aryl (including heteroaryl). In an alternative embodiment, R_4 is selected from substituted alkyl, particularly haloalkyl (including CF_3) and arylalkyl (including heteroarylalkyl). In an alternative embodiment, R_4 is selected from unsubstituted C_{1-8} alkyl (preferably saturated C_{1-6} alkyl).

In one embodiment R_4 is selected from H, alkyl (including arylalkyl (including heteroarylalkyl)), halogen, COR_5, CO_2R_5, $CONR_6R_7$ and $CONR_5NR_6R_7$, preferably from H, alkyl (including arylalkyl (including heteroarylalkyl)) and halogen, and preferably from H.

In the compounds of formula (I), R_5, R_6 and R_7 are independently selected from H, alkyl (including branched and unbranched alkyl, substituted and unsubstituted alkyl, cyclic and acyclic alkyl) and aryl (including heteroaryl), or where R_6 and R_7 are in any NR_6R_7 group R_6 and R_7 may be linked to form a heterocyclic group, or where R_5, R_6 and R_7 are in a $CONR_5NR_6R_7$ group, R_5 and R_6 may be linked to form a heterocyclic group.

In the compounds of formula (I), R_{12} and R_{13} are independently selected from H, alkyl (including branched and unbranched alkyl, substituted and unsubstituted alkyl, cyclic and acyclic alkyl) and aryl (including heteroaryl), or where R_{12} and R_{13} are in any $NR_{12}R_{13}$ group

R_{12} and R_{13} may be linked to form a heterocyclic group, or where R_5, R_{12} and R_{13} are in a $CONR_5NR_{12}R_{13}$ group, R_5 and R_{12} may be linked to form a heterocyclic group.

In the compounds of formula (I), R_8 is selected from alkyl (including branched and unbranched alkyl, substituted and unsubstituted alkyl, cyclic and acyclic alkyl) and aryl (including heteroaryl).

Where R_5 to R_{10}, R_{12} and R_{13}, are independently selected from alkyl, preferably R_5 to R_{10}, R_{12} and R_{13} are independently selected from C_{1-6} alkyl, preferably C_{1-6} saturated alkyl and more preferably from lower alkyl.

Where R_6 and R_7, or R_{12} and R_{13}, are linked to form a heterocyclic ring, said heterocyclic ring may be saturated, partially unsaturated or aromatic, and is preferably saturated. Said heterocyclic ring is preferably a 5, 6 or 7-membered ring, preferably a 5 or 6-membered ring, and may contain one or more further heteroatom(s) preferably selected from N, O and S.

Where R_5 and R_6, or R_5 and R_{12}, are linked to form a heterocyclic ring, said heterocyclic ring may be saturated, partially unsaturated or aromatic, and is preferably saturated. Said heterocyclic ring is preferably a 5, 6 or 7-membered ring, preferably a 5 or 6-membered ring, and may contain one or more further heteroatom(s) preferably selected from N, O and S.

In a particularly preferred embodiment of the invention, the compounds of the present invention are selected from:
7-bromo-4-(2-furyl)-N-(2-hydroxyethyl)thieno[3,2-d]pyrimidine-2-amine;
N-allyl-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine;
2-ethyl-4-(2-pyridyl)thieno[3,2-d]pyrimidine;
2-methyl-4-(2-pyridyl)thieno[3,2-d]pyrimidine;
2-*n*-propyl-4-(2-pyridyl)thieno[3,2-d]pyrimidine;
N-(2-hydroxyethyl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine;
2-isopropyl-4-(2-pyridyl)thieno[3,2-d]pyrimidine;
N-(2-methoxyethyl)-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine;
N,N-dimethyl-4-(4-methyl-2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine;
4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine;

2-ethyl-4-(4-methyl-2-thiazolyl)thieno[3,2-d]pyrimidine;
2-ethyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine;
N,N-dimethyl-4-(5-methyl-2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine;
N,N-dimethyl-4-(4,5-dimethyl-2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine;
4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine;
(2R)-2-(2-hydroxymethylpyrrolidin-1-yl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine;
N-allyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine;
2-isopropyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine;
N,N-dimethyl-4-(5-methyl-2-pyridyl)thieno[3,2-d]pyrimidine-2-amine;
2-*tert*-butyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine;
2-cyclopropyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine;
2-ethyl-4-(6-methyl-2-pyridyl)thieno[3,2-d]pyrimidine;
(2S)-2-(2-hydroxymethylpyrrolidin-1-yl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine; and
2-(2-chloroethyl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine.

Where chiral the compounds of the present invention may be in the form of a racemic mixture of pairs of enantiomers or in enantiomerically pure form.

According to a further aspect of the invention, there is provided for use in therapy a compound of the present invention, or a pharmaceutically acceptable salt or prodrug thereof.

The present invention may be employed in respect of a human or animal subject, more preferably a mammal, more preferably a human subject.

The disorders of particular interest are those in which the blocking of purine receptors, partiucularly adenosine receptors and more particularly adenosine A_{2A} receptors, may be beneficial. These may include movement disorders such as Parkinson's disease, drug-induced Parkinsonism, post-encephalitic Parkinsonism, Parkinsonism induced by poisoning (for example MPTP, manganese, carbon monoxide) and post-traumatic Parkinson's disease (punch-drunk syndrome).

Other movement disorders in which the blocking of purine receptors, may be of benefit include progressive supernuclear palsy, Huntingtons disease, multiple system atrophy, corticobasal degeneration, Wilsons disease, Hallerrorden-Spatz disease, progressive pallidal atrophy, Dopa-responsive dystonia-Parkinsonism, spasticity or other disorders of the basal ganglia which result in abnormal movement or posture. The present invention may also be effective in treating Parkinson's with on-off phenomena; Parkinson's with freezing (end of dose deterioration); and Parkinson's with prominent dyskinesias.

The compounds of formula (I) may be used or administered in combination with one or more additional drugs useful in the treatment of movement disorders, such as L-DOPA or a dopamine agonist, the components being in the same formulation or in separate formulations for administration simultaneously or sequentially.

Other disorders in which the blocking of purine receptors, particularly adenosine receptors and more particularly adenosine A_{2A} receptors may be beneficial include acute and chronic pain; for example neuropathic pain, cancer pain, trigeminal neuralgia, migraine and other conditions associated with cephalic pain, primary and secondary hyperalgesia, inflammatory pain, nociceptive pain, tabes dorsalis, phantom limb pain, spinal cord injury pain, central pain, post-herpetic pain and HIV pain; affective disorders including mood disorders such as bipolar disorder, seasonal affective disorder, depression, manic depression, atypical depression and monodepressive disease; central and peripheral nervous system degenerative disorders including corticobasal degeneration, demyelinating disease (multiple sclerosis, disseminated sclerosis), Freidrich's ataxia, motoneurone disease (amyotrophic lateral sclerosis, progressive bulbar atrophy), multiple system atrophy, myelopathy, radiculopathy, peripheral neuropathy (diabetic neuropathy, tabes dorsalis, drug-induced neuropathy, vitamin deficiency), systemic lupus erythamatosis, granulomatous disease, olivo-ponto-cerebellar atrophy, progressive pallidal atrophy, progressive supranuclear palsy, spasticity; schizophrenia and related pyshoses; cognitive disorders including dementia, Alzheimers Disease, Frontotemporal dementia, multi-infarct dementia, AIDS dementia, dementia associated with Huntingtons Disease, Lewy body dementia, senile dementia, age-related memory impairment, cognitive impairment associated with dementia, Korsakoff syndrome, dementia pugilans; attention disorders such as attention-deficit hyperactivity disorder (ADHD), attention deficit disorder, minimal brain

dysfunction, brain-injured child syndrome, hyperkinetic reaction childhood, and hyperactive child syndrome; central nervous system injury including traumatic brain injury, neurosurgery (surgical trauma), neuroprotection for head injury, raised intracranial pressure, cerebral oedema, hydrocephalus, spinal cord injury; cerebral ischaemia including transient ischaemic attack, stroke (thrombotic stroke, ischaemic stroke, embolic stroke, haemorrhagic stroke, lacunar stroke) subarachnoid haemorrhage, cerebral vasospasm, neuroprotection for stroke, peri-natal asphyxia, drowning, cardiac arrest, subdural haematoma; myocardial ischaemia; muscle ischaemia; sleep disorders such as hypersomnia and narcolepsy; eye disorders such as retinal ischaemia-reperfusion injury and diabetic neuropathy; cardiovascular disorders such as claudication and hypotension; and diabetes and its complications.

According to a further aspect of the present invention, there is provided the use of a compound of the present invention or a pharmaceutically acceptably salt or prodrug thereof in the manufacture of a medicament for the treatment or prevention of a disorder in which the blocking of purine receptors, particularly adenosine receptors and more particularly A_{2A} receptors, may be beneficial.

According to a further aspect of the present invention there is provided a method of treating or preventing a disorder in which the blocking of purine receptors, particularly adenosine receptors and more particularly adenosine A_{2A} receptors, may be beneficial, the method comprising administration to a subject in need of such treatment an effective dose of a compound of the present invention or a pharmaceutically acceptable salt or prodrug thereof.

The disorder may be caused by the hyperfunctioning of the purine receptors.

According to a further aspect of the present invention there is provided use of a compound of the present invention or a pharmaceutically acceptable salt or prodrug thereof in the manufacture of a medicament for the treatment or prevention of movement disorders in a subject.

According to a further aspect of the invention there is provided a method of treating or preventing movement disorders comprising administration to a subject in need of such

treatment an effective dose of a compound of the present invention or a pharmaceutically acceptable salt or prodrug thereof.

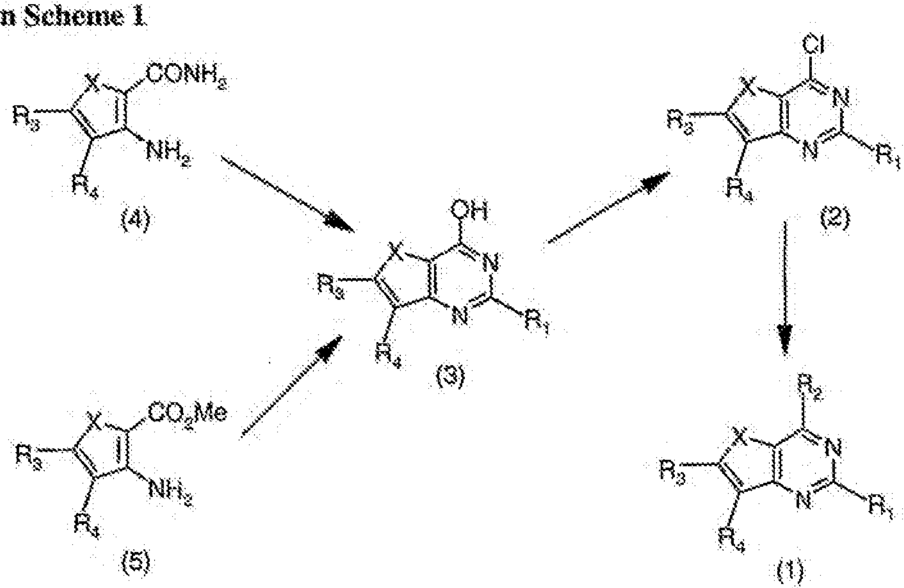
According to a further aspect of the invention there is provided use of a compound of the present invention or a pharmaceutically acceptable salt or prodrug thereof in the manufacture of a medicament for neuroprotection in a subject.

According to a further aspect of the invention there is provided a method of neuroprotection comprising administration to a subject in need of such treatment an effective dose of a compound of the present invention or a pharmaceutically acceptable salt or prodrug thereof.

The medicament for or method of neuroprotection may be of use in the treatment of subjects who are suffering from or at risk from a neurodegenerative disorder, such as a movement disorder.

According to a further aspect of the invention, there is provided a method of preparing the novel compounds of the present invention. Compounds of formula (I) may be prepared according to conventional synthetic methods, such as set out in Reaction Scheme 1.

Reaction Scheme 1



Compounds of formula (1) are prepared from halides of formula (2) by standard methods such as aryl coupling reactions which may be advantageously carried out in the presence of

a catalyst such as a palladium catalyst. The aryl coupling reaction may be carried out by reaction of a halide of formula (2) with, for example, an aryl or heteroaryl trialkyltin reagent, an aryl or heteroaryl boronic acid or boronic ester reagent or an aryl or heteroaryl zinc halide reagent according to methods described in the literature. Suitable aryl or heteroaryl trialkyl tin, boronic acid, boronic ester or zinc halide reagents are either commercially available or may be prepared by standard literature methods.

Halides of formula (2) are either known in the literature or may be prepared from compounds of formula (3) by standard methods, for example by treatment with a chlorinating reagent such as $POCl_3$. Compounds of formula (3) are either known in the literature or may be prepared from compounds of formula (4) by standard methods such as treatment with an appropriate ester (R_1CO_2Et) in the presence of a suitable base such as NaOEt, or by treatment with an appropriate anhydride $(R_1CO)_2O$ in the presence of a base such as Et_3N followed by heating in the presence of a stronger base such as NaOH. Alternatively compounds of formula (3) may be prepared from compounds of formula (5) by standard methods such as treatment with an appropriate nitrile (R_1CN) in the presence of dry HCl gas. Compounds of formula (4) and formula (5) are either known in the literature or may be prepared by standard methods.

Compounds of formula (1) where R_1 is NR_6R_7 may be prepared from compounds of formula (1) where R_1 is halogen by standard methods such as reaction with an appropriate amine (R_6R_7NH). Compounds of formula (1) where R_1 is halogen may be prepared from compounds of formula (2) where R_1 is halogen as described above. Compounds of formula (2) where R_1 is halogen are either known in the literature or may be prepared by methods analogous to those described in the literature.

Compounds of formula (1) where R_1 is $NR_5CONR_6R_7$, NR_5COR_6, $NR_5CO_2R_8$ or $NR_5SO_2R_8$ wherein R_5 is H may be prepared from compounds of formula (1) where R_1 is NH_2 by standard methods for example by treatment with an appropriate isocyanate (R_6NCO or R_7NCO), carbamoyl chloride (R_6R_7NCOCl), acid chloride (R_6COCl), chloroformate ($ClCO_2R_8$) or sulphonyl chloride ($ClSO_2R_8$). Analogous compounds wherein R_5 is alkyl may be prepared by initial alkylation or reductive alkylation followed by reaction with the appropriate reagent as described above.

Compounds of formula (1) where R_1 is NH_2 may be prepared from compounds of formula (1) where R_1 is halogen either by direct displacement with ammonia or by reaction with an appropriate protected amine, for example 3,4-dimethoxybenzylamine, followed by removal of the protecting group, if desired, by treatment with TFA.

Compounds of formula (1) where R_1 is hydroxy, alkoxy, aryloxy, thioalkyl, thioaryl, or CN may be prepared from compounds of formula (1) where R_1 is halogen by direct displacement with an appropriate nucleophile such as water, an alcohol, thiol or cyanide in the presence of a suitable base.

Compounds of formula (1) where R_1 is $CONR_6R_7$ or $CONR_5NR_6R_7$ may be prepared from compounds of formula (1) where R_1 is CO_2R_5 by standard methods such as reaction with an appropriate amine (R_6R_7NH) or substituted hydrazine ($HNR_5NR_6R_7$), either directly or in the presence of a suitable reagent such as trimethylaluminium.

Compounds of formula (1) where R_1 is COR_5, wherein R_5 is H, may be prepared from compounds of formula (1) where R_1 is CO_2R_5 by standard methods such as reduction with an appropriate reducing agent such as DIBAL at low temperature. Compounds of formula (1) where R_1 is COR_5, wherein R_5 is alkyl or aryl, may be prepared from compounds of formula (1) where R_1 is COR_5, wherein R_5 is H, by standard methods such as initial treatment with an appropriate alkyl or aryllithium or Grignard reagent, followed by oxidation.

Compounds of formula (1) where R_1 is CO_2R_5 may be prepared according to Reaction Scheme 1 by the methods described above.

In a compound of formula (1) where R_1 is alkyl or aryl or where the group R_1 contains an alkyl or aryl substituent, the alkyl or aryl group may be substituted as defined above. Where the alkyl or aryl group is substituted by a reactive functional group it will be appreciated that derivatisation of the reactive functional group may lead to a wide variety of additional substituent groups. By way of example where the alkyl or aryl group is substituted by an amino group then the amino group may be derivatised to form a mono- or dialkylamine,

urea, thiourea, amide, carbamate or sulphonamide by the use of standard reactions such as those described above. Where the alkyl or aryl group is substituted by an amino group it may be advantageous to protect the amino group during the synthesis by the use of a standard protecting group such as a BOC group. The protecting group may then be removed at the appropriate step in the synthesis, by standard methods such as treatment with TFA.

Compounds of formula (1) where R_3 is halogen or NO_2 may be prepared from compounds of formula (2) where R_3 is halogen or NO_2 as described above. Compounds of formula (2) where R_3 is halogen or NO_2 are either known in the literature or may be prepared from compounds of formula (2) where R_3 is H by standard literature methods such as halogenation or nitration.

Compounds of formula (1) where R_3 is hydroxy, alkoxy or cyano may be prepared from compounds of formula (2) where R_3 is hydroxy, alkoxy or cyano as described above. Compounds of formula (2) where R_3 is hydroxy, alkoxy or cyano may be prepared from compounds of formula (2) where R_3 is halogen by standard literature methods such as nucleophilic displacement.

Compounds of formula (1) where R_4 is aryl or heteroaryl may be prepared from compounds of formula (1) where R_4 is halogen by standard methods such as palladium catalysed aryl coupling reactions as described above. Compounds of formula (1) where R_4 is halogen are prepared from compounds of formula (2) where R_4 is halogen as described above. Compounds of formula (2) where R_4 is halogen are either known in the literature or prepared by methods analogous to those described in the literature.

Compounds of formula (1) where R_4 is NH_2 are prepared from compounds of formula (1) where R_4 is NO_2 by standard methods such as reduction. Compounds of formula (1) where R_4 is NO_2 are prepared from compounds of formula (2) where R_4 is NO_2 as described above. Compounds of formula (2) where R_4 is NO_2 are either known in the literature or prepared by methods analogous to those described in the literature.

Compounds of formula (1) where R_4 is NR_6R_7, $NR_5CONR_6R_7$, NR_5COR_6, $NR_5CO_2R_8$ or $NR_5SO_2R_8$ wherein R_5 is H may be prepared from compounds of formula (1) where R_4 is NH_2 by standard methods for example by mono- or dialkylation, reductive alkylation or by treatment with an appropriate isocyanate (R_6NCO or R_7NCO), carbamoyl chloride (R_6R_7NCOCl), acid chloride (R_6COCl), chloroformate ($ClCO_2R_8$) or sulphonyl chloride ($ClSO_2R_8$). Analogous compounds wherein R_5 is alkyl may be prepared by initial alkylation or reductive alkylation followed by reaction with the appropriate reagent as described above.

Compounds of formula (1) where R_4 is COR_5 may be prepared from compounds of formula (2) where R_4 is COR_5 as described above. Compounds of formula (2) where R_1 is COR_5 may be prepared from compounds of formula (2) where R_4 is H by standard methods such as Friedel-Crafts acylation.

Compounds of formula (1) where R_4 is CO_2R_5, $CONR_6R_7$ or $CONR_5NR_6R_7$ may be prepared from compounds of formula (2) where R_4 is CO_2R_5, $CONR_6R_7$ or $CONR_5NR_6R_7$ as described above. Compounds of formula (2) where R_4 is CO_2R_5 or $CONR_6R_7$ may be prepared from compounds of formula (2) where R_4 is halogen by standard methods such as palladium catalysed carbonylation reactions in the presence of an appropriate alcohol (R_5OH) or amine (HNR_6R_7). Compounds of formula (2) where R_4 is $CONR_6R_7$ or $CONR_5NR_6R_7$ may be prepared from compounds of formula (2) where R_4 is CO_2R_5 by standard methods such as reaction with a suitable amine (HNR_6R_7) or hydrazine ($HNR_5NR_6R_7$) derivative.

Compounds of formula (1) where R_4 is cyano may be prepared from compounds of formula (1) where R_4 is $CONR_6R_7$, wherein R_6 and R_7 are both H, by standard literature methods such as dehydration.

Compounds of formula (1) where R_4 is hydroxy, alkoxy, aryloxy, thioalkyl or thioaryl may be prepared by standard literature methods known to those skilled in the art. Such standard methods may include treatment of a compound of formula (1) where R_4 is halogen with an appropriate nucleophile. Alternatively compounds of formula (1) where R_4 is hydroxy or alkoxy may be prepare from a compound of formula (1) where R_4 is COR_5 by use of the

Bayer Villiger reaction, followed by a hydrolysis step and followed, if desired, by an alkylation step.

According to a further aspect of the invention, there is provided a pharmaceutical composition comprising a compound of the present invention in combination with a pharmaceutically acceptable carrier or excipient and a method of making such a composition comprising combining a compound of the present invention with a pharmaceutically acceptable carrier or excipient.

The pharmaceutical compositions employed in the present invention comprise a compound of the present invention, or pharmaceutically acceptable salts or prodrugs thereof, and may also contain a pharmaceutically acceptable carrier and optionally other therapeutic ingredients known to those skilled in the art. The term, "pharmaceutically acceptable salts", refers to salts prepared from pharmaceutically acceptable non-toxic acids including inorganic acids and organic acids.

Where the compounds of the present invention are basic, salts may be prepared from pharmaceutically acceptable non-toxic acids including inorganic and organic acids. Such acids include acetic, benzenesulfonic, benzoic, camphorsulfonic, citric, ethenesulfonic, fumaric, gluconic, glutamic, hippuric, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, mandelic, methanesulfonic, mucic, nitric, pamoic, pantothenic, phosphoric, succinic, sulfuric, tartaric, oxalic, p-toluenesulfonic and the like. Particularly preferred are hydrochloric, hydrobromic, phosphoric, and sulfuric acids, and most particularly preferred is the hydrochloride salt.

Any suitable route of administration may be employed for providing the patient with an effective dosage of a compound of the present invention. For example, oral, rectal, parenteral (intravenous, intramuscular), transdermal, subcutaneous, and the like may be employed. Dosage forms include tablets, troches, dispersions, suspensions, solutions, capsules, patches, and the like. The most suitable route in any given case will depend on the severity of the condition being treated. The most preferred route of administration of the present invention is the oral route. The compositions may be conveniently presented in unit dosage form and prepared by any of the methods well known in the art of pharmacy.

In practical use, the compounds of the present invention can be combined as the active ingredient in intimate admixture with a pharmaceutical carrier according to conventional pharmaceutical compounding techniques. The carrier may take a wide variety of forms depending on the form of preparation desired for administration, *e.g.* oral or parenteral (*e.g.* intravenous). In preparing the compositions for oral dosage form, any of the usual pharmaceutical media may be employed as carriers, such as, for example, water, glycols, oils, alcohols, flavouring agents, preservatives, colouring agents, and the like in the case of oral liquid preparations (such as suspensions, solutions and elixirs) or aerosols; or carriers such as starches, sugars, micro-crystalline cellulose, diluents, granulating agents, lubricants, binders, disintegrating agents, and the like may be used in the case of oral solid preparations such as, for example, powders, capsules, and tablets, with the solid oral preparations being preferred over the liquid preparations. The most preferred solid oral preparation is tablets.

Because of their ease of administration, tablets and capsules represent the most advantageous oral dosage unit form in which case solid pharmaceutical carriers are employed. If desired, tablets may be coated by standard aqueous or non-aqueous techniques.

In addition to the common dosage forms set out above, the compounds of the present invention may also be administered by controlled release means and/or delivery devices such as those described in United States Patent Nos.: 3,845,770; 3,916,899; 3,536,809; 3,598,123; 3,630,200; 4,008,719; 4,687,660; and 4,769,027, the disclosures of which are hereby incorporated by reference.

Pharmaceutical compositions employed in the present invention suitable for oral administration may be presented as discrete units such as capsules, cachets, or tablets, or aerosol sprays each containing a predetermined amount of the active ingredient as a powder or granules, a solution or a suspension in an aqueous liquid, an oil-in-water emulsion, or a water-in-oil liquid emulsion. Such compositions may be prepared by any of the methods of pharmacy, but all methods include the step of bringing the active ingredient into association with the carrier which constitutes one or more necessary ingredients. In general, the

compositions are prepared by uniformly and intimately admixing the active ingredient with liquid carriers or finely divided solid carriers or both, and then, if necessary, shaping the product into the desired presentation.

For example, a tablet may be prepared by compression or moulding, optionally with one or more accessory ingredients. Compressed tablets may be prepared by compressing in a suitable machine the active ingredient in a free-flowing form such as powder or granules, optionally mixed with a binder, a lubricant, an inert diluent, and/or a surface active or dispersing agent. Moulded tablets may be made by moulding in a suitable machine a mixture of the powdered compound moistened with an inert liquid diluent.

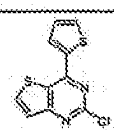
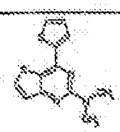
The invention is further defined by reference to the following examples. It will be apparent to those skilled in the art that many modifications, both to materials and methods, may be practised without departing from the purpose and interest of this invention.

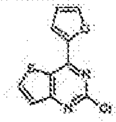
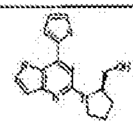
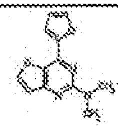
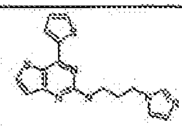
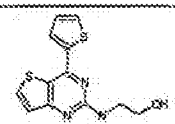
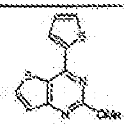
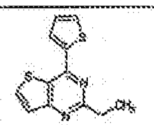
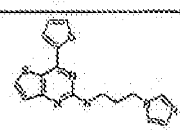
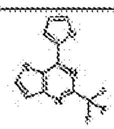
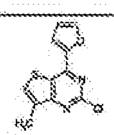
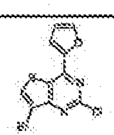
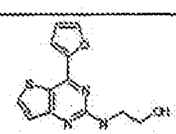
EXAMPLES

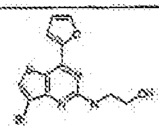
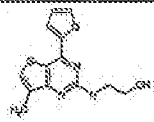
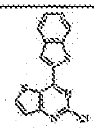
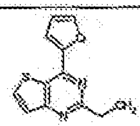
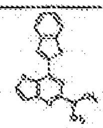
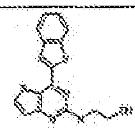
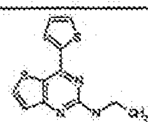
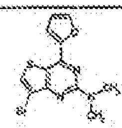
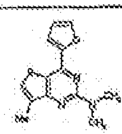
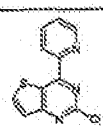
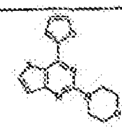
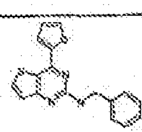
Synthetic Examples

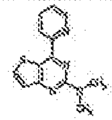
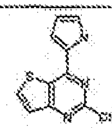
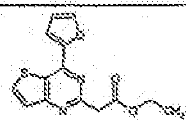
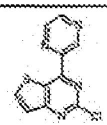
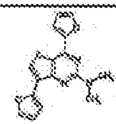
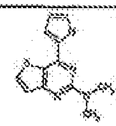
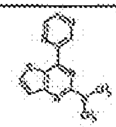
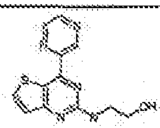
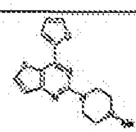
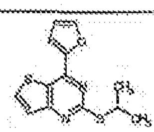
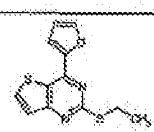
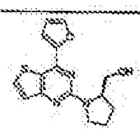
The invention is illustrated with reference to the following Examples, as set out in Table 1. The syntheses of the Examples are performed using the general Synthetic Methods described hereinafter. The Method used for each Example is given in parentheses in column 1 of Table 1. Analytical data are given in Table 2.

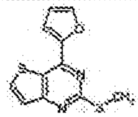
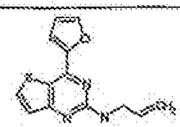
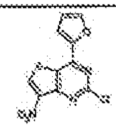
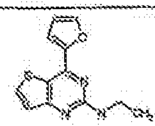
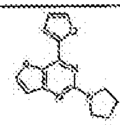
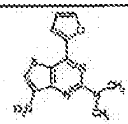
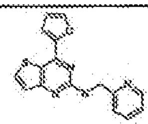
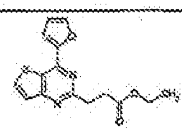
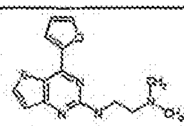
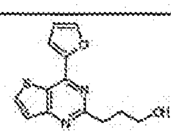
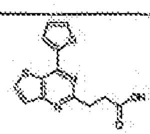
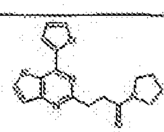
Table 1

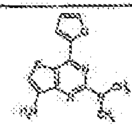
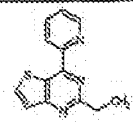
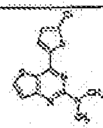
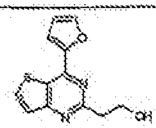
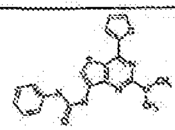
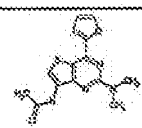
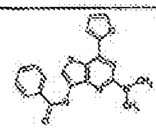
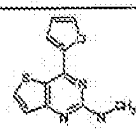
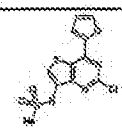
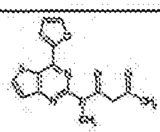
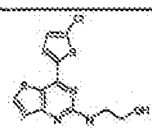
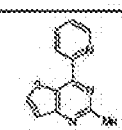
Example	Structure	Compound Name
1 (A)		2-chloro-4-(2-thienyl)thieno[3,2-d]pyrimidine
2 (E)		N,N-dimethyl-4-(2-thienyl)thieno[3,2-d]pyrimidine-2-amine

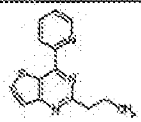
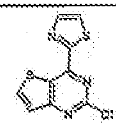
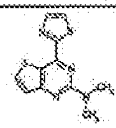
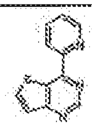
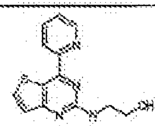
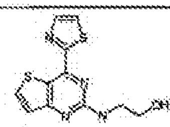
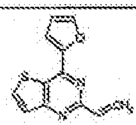
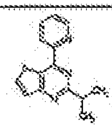
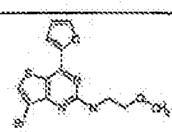
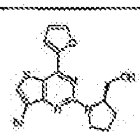
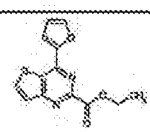
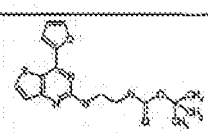
3 (A)		2-chloro-4-(2-furyl)thieno[3,2-d]pyrimidine
4 (E)		(2R)-2-(2-hydroxymethylpyrrolidin-1-yl)-4-(2-thienyl)thieno[3,2-d]pyrimidine
5 (E)		N,N-dimethyl-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine
6 (E)		N-(3-(1H-imidazol-1-yl)propyl)-4-(2-thienyl)thieno[3,2-d]pyrimidine-2-amine
7 (E)		N-(2-hydroxyethyl)-4-(2-thienyl)thieno[3,2-d]pyrimidine-2-amine
8 (E)		2-methoxy-4-(2-thienyl)thieno[3,2-d]pyrimidine
9 (B)		2-ethyl-4-(2-thienyl)thieno[3,2-d]pyrimidine
10 (E)		N-(3-(1H-imidazol-1-yl)propyl)-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine
11 (A)		4-(2-furyl)-2-trifluoromethylthieno[3,2-d]pyrimidine
12 (A)		2-chloro-4-(2-furyl)-7-methylthieno[3,2-d]pyrimidine
13 (A)		7-bromo-2-chloro-4-(2-furyl)thieno[3,2-d]pyrimidine
14 (E)		4-(2-furyl)-N-(2-hydroxyethyl)thieno[3,2-d]pyrimidine-2-amine

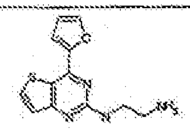
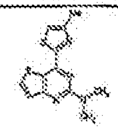
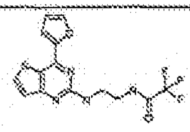
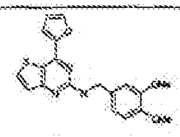
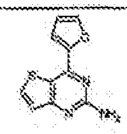
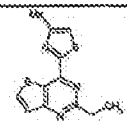
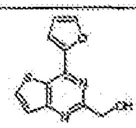
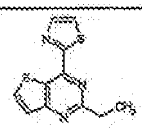
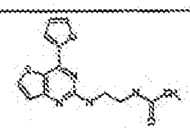
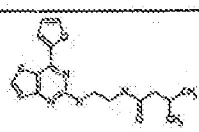
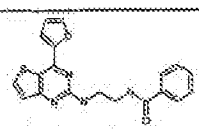
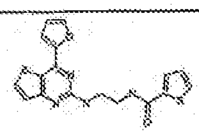
15 (E)		7-bromo-4-(2-furyl)-N-(2-hydroxyethyl)thieno[3,2-d]pyrimidine-2-amine
16 (E)		4-(2-furyl)-N-(2-hydroxyethyl)-7-methylthieno[3,2-d]pyrimidine-2-amine
17 (A)		4-(2-benzothiophenyl)-2-chlorothieno[3,2-d]pyrimidine
18 (A)		2-ethyl-4-(2-furyl)thieno[3,2-d]pyrimidine
19 (E)		4-(2-benzothiophenyl)-N,N-dimethylthieno[3,2-d]pyrimidine-2-amine
20 (E)		4-(2-benzothiophenyl)-N-(2-hydroxyethyl)thieno[3,2-d]pyrimidine-2-amine
21 (E)		N-ethyl-4-(2-thienyl)thieno[3,2-d]pyrimidine-2-amine
22 (E)		7-bromo-N,N-dimethyl-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine
23 (E)		4-(2-furyl)-7,N,N-trimethylthieno[3,2-d]pyrimidine-2-amine
24 (A)		2-chloro-4-(2-pyridyl)thieno[3,2-d]pyrimidine
25 (E)		4-(2-furyl)-2-morpholinothieno[3,2-d]pyrimidine
26 (E)		N-benzyl-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine

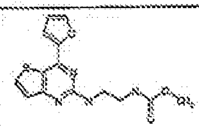
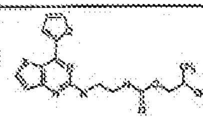
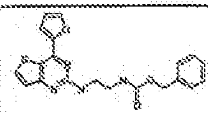
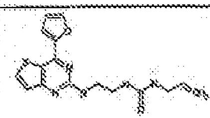
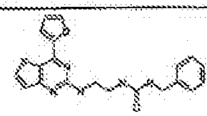
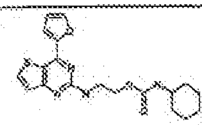
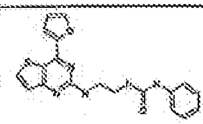
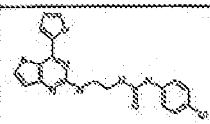
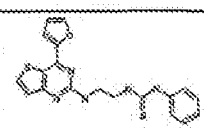
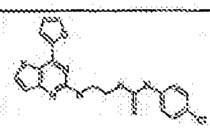
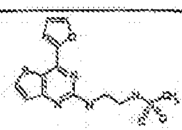
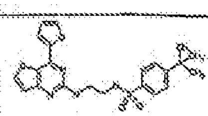
27 (E)		N,N-dimethyl-4-(2-pyridyl)thieno[3,2-d]pyrimidine-2-amine
28 (B)		2-chloro-4-(1H-pyrrol-1-yl)thieno[3,2-d]pyrimidine
29 (A)		Ethyl 4-(2-furyl)thieno[3,2-d]pyrimidine-2-acetate
30 (A)		2-chloro-4-(2-pyrazinyl)thieno[3,2-d]pyrimidine
31 (P)		4,7-bis(2-furyl)-N,N-dimethylthieno[3,2-d]pyrimidine-2-amine
32 (E)		N,N-dimethyl-4-(1H-pyrrol-1-yl)thieno[3,2-d]pyrimidine-2-amine
33 (E)		N,N-dimethyl-4-(2-pyrazinyl)thieno[3,2-d]pyrimidine-2-amine
34 (E)		N-(2-hydroxyethyl)-4-(2-pyrazinyl)thieno[3,2-d]pyrimidine-2-amine
35 (E)		4-(2-furyl)--2-(4-methylpiperazinyl)thieno[3,2-d]pyrimidine
36 (E)		4-(2-furyl)--2-isopropylthiothieno[3,2-d]pyrimidine
37 (E)		2-ethylthio-4-(2-furyl)thieno[3,2-d]pyrimidine
38 (E)		(2R)-4-(2-furyl)-2-(2-hydroxymethylpyrrolidin-1-yl)thieno[3,2-d]pyrimidine

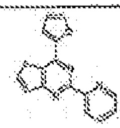
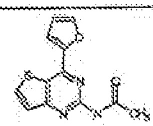
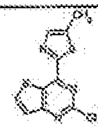
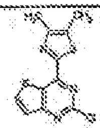
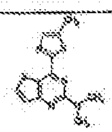
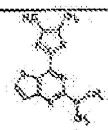
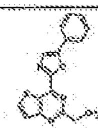
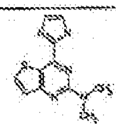
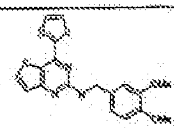
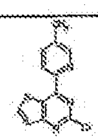
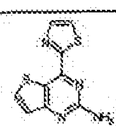
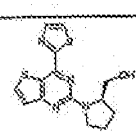
39 (E)		4-(2-furyl)-2-methylthiothieno[3,2-d]pyrimidine
40 (E)		N-allyl-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine
41 (A)		2-chloro-4-(2-furyl)-7-nitrothieno[3,2-d]pyrimidine
42 (E)		N-ethyl-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine
43 (E)		4-(2-furyl)-2-(pyrrolidin-1-yl)thieno[3,2-d]pyrimidine
44 (E)		N,N-dimethyl-4-(2-furyl)-7-nitrothieno[3,2-d]pyrimidine-2-amine
45 (E)		4-(2-furyl)-N-(2-pyridylmethyl)thieno[3,2-d]pyrimidine-2-amine
46 (A)		Ethyl 3-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-yl)propionate
47 (E)		N-(2-dimethylaminoethyl)-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine
48 (K)		3-(4-(2-furyl)thieno[3,2-d]pyrimidin-2-yl)propanol
49 (M)		3-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-yl)propionic acid
50 (N)		4-(2-furyl)-2-(3-oxo-3-(1-pyrrolidinyl)propyl)thieno[3,2-d]pyrimidine

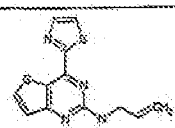
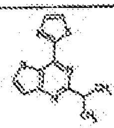
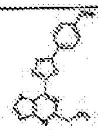
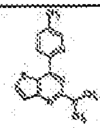
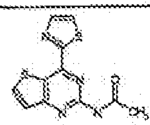
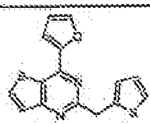
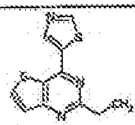
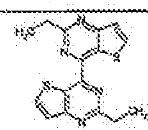
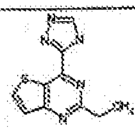
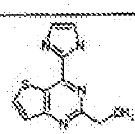
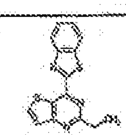
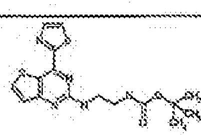
51 (J)		7-amino-N,N-dimethyl-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine
52 (C)		2-ethyl-4-(2-pyridyl)thieno[3,2-d]pyrimidine
53 (E)		4-(5-chloro-2-thienyl)-N,N-dimethylthieno[3,2-d]pyrimidine-2-amine
54 (K)		2-(4-(2-furyl)thieno[3,2-d]pyrimidin-2-yl)ethanol
55 (I)		N-(2-dimethylamino-4-(2-furyl)thieno[3,2-d]pyrimidine-7-yl)-N'-phenylurea
56 (G)		N-(2-dimethylamino-4-(2-furyl)thieno[3,2-d]pyrimidine-7-yl)acetamide
57 (G)		N-(2-dimethylamino-4-(2-furyl)thieno[3,2-d]pyrimidine-7-yl)benzamide
58 (E)		4-(2-furyl)-N-methylthieno[3,2-d]pyrimidine-2-amine
59 (G)		N-(2-chloro-4-(2-furyl)thieno[3,2-d]pyrimidine-7-yl)methanesulphonamide
60 (G)		N-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-yl)-N-methyl-3-oxobutanamide
61 (E)		4-(5-chloro-2-thienyl)-N-(2-hydroxyethyl)thieno[3,2-d]pyrimidine-2-amine
62 (C)		2-methyl-4-(2-pyridyl)thieno[3,2-d]pyrimidine

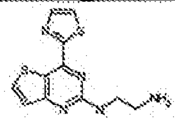
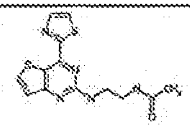
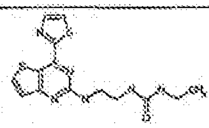
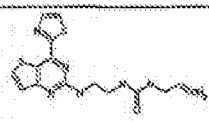
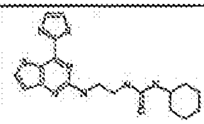
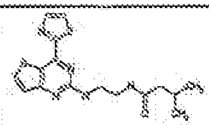
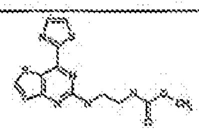
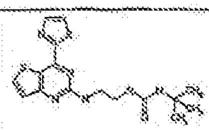
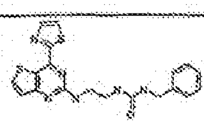
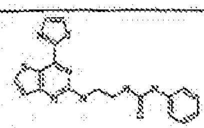
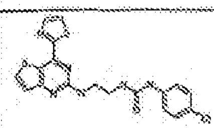
63 (C)		2-*n*-propyl-4-(2-pyridyl)thieno[3,2-d]pyrimidine
64 (C)		2-chloro-4-(2-thiazolyl)thieno[3,2-d]pyrimidine
65 (E)		N,N-dimethyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine
66 (C)		4-(2-pyridyl)thieno[3,2-d]pyrimidine
67 (E)		N-(2-hydroxyethyl)-4-(2-pyridyl)thieno[3,2-d]pyrimidine-2-amine
68 (E)		N-(2-hydroxyethyl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine
69 (L)		4-(2-furyl)-2-vinylthieno[3,2-d]pyrimidine
70 (C)		2-isopropyl-4-(2-pyridyl)thieno[3,2-d]pyrimidine
71 (E)		N-(2-methoxyethyl)-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine
72 (E)		(2R)-7-bromo-4-(2-furyl)-2-(2-hydroxymethylpyrrolidin-1-yl)thieno[3,2-d]pyrimidine
73 (A)		Ethyl 4-(2-furyl)thieno[3,2-d]pyrimidine-2-carboxylate
74 (E)		*tert*-butyl (2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)carbamate

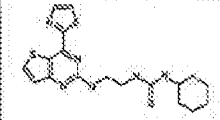
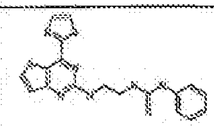
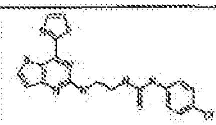
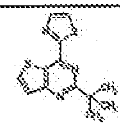
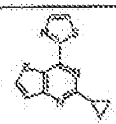
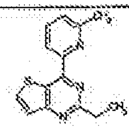
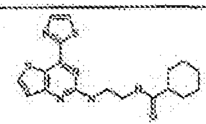
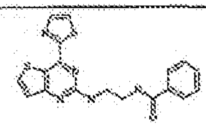
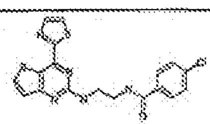
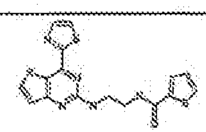
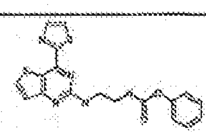
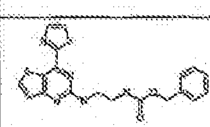
75 (F)		N-(2-aminoethyl)-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine
76 (E)		N,N-dimethyl-4-(4-methyl-2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine
77 (H)		N-(2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)trifluoroacetamide
78 (E)		N-(3,4-dimethoxybenzyl)-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine
79 (F)		4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine
80 (C)		2-ethyl-4-(4-methyl-2-thiazolyl)thieno[3,2-d]pyrimidine
81 (K)		4-(2-furyl)thieno[3,2-d]pyrimidine-2-methanol
82 (C)		2-ethyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine
83 (H)		N-(2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)acetamide
84 (H)		N-(2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)-3-methylbutanamide
85 (H)		N-(2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)benzamide
86 (H)		N-(2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)thiophene-2-carboxamide

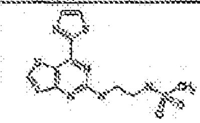
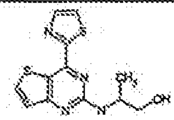
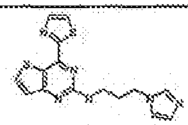
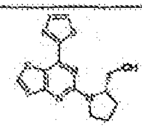
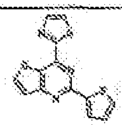
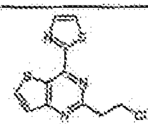
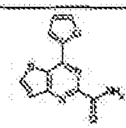
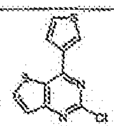
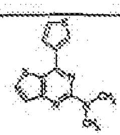
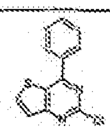
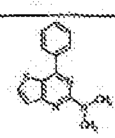
87 (H)		methyl (2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)carbamate
88 (H)		isobutyl (2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)carbamate
89 (H)		benzyl (2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)carbamate
90 (H)		9-fluorenylmethyl (2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)carbamate
91 (I)		N-allyl-N'-(2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)urea
92 (I)		N-benzyl-N'-(2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)urea
93 (I)		N-cyclohexyl-N'-(2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)urea
94 (I)		N-(2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)-N'-phenylurea
95 (I)		N-(4-chlorophenyl)-N'-(2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)urea
96 (I)		N-(2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)-N'-phenylthiourea
97 (I)		N-(4-chlorophenyl)-N'-(2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)thiourea
98 (H)		N-(2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)methanesulphonamide
99 (H)		N-(2-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)-4-*tert*-butylphenylsulphonamide

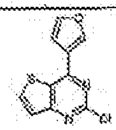
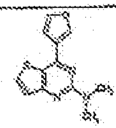
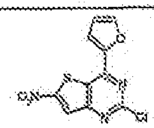
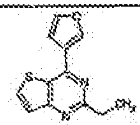
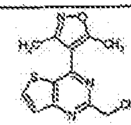
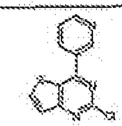
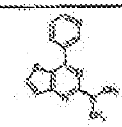
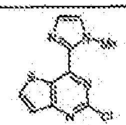
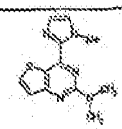
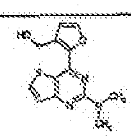
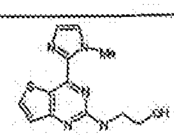
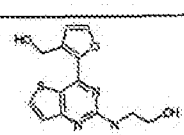
100 (A)		4-(2-furyl)-2-(2-pyridyl)thieno[3,2-d]pyrimidine
101 (G)		N-(4-(2-furyl)thieno[3,2-d]pyrimidin-2-yl)acetamide
102 (C)		2-chloro-4-(5-methyl-2-thiazolyl)thieno[3,2-d]pyrimidine
103 (C)		2-chloro-4-(4,5-dimethyl-2-thiazolyl)thieno[3,2-d]pyrimidine
104 (E)		N,N-dimethyl-4-(5-methyl-2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine
105 (E)		N,N-dimethyl-4-(4,5-dimethyl-2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine
106 (C)		2-ethyl-4-(5-phenyl-2-oxazolyl)thieno[3,2-d]pyrimidine
107 (D)		N,N-dimethyl-4-(1H-imidazol-2-yl)thieno[3,2-d]pyrimidine-2-amine
108 (E)		N-(3,4-dimethoxybenzyl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine
109 (C)		2-chloro-4-(5-methyl-2-pyridyl)thieno[3,2-d]pyrimidine
110 (F)		4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine
111 (E)		(2R)-2-(2-hydroxymethylpyrrolidin-1-yl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine

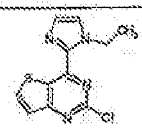
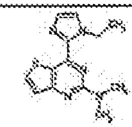
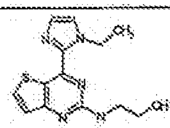
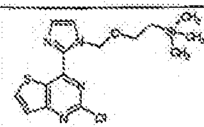
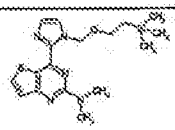
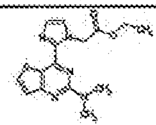
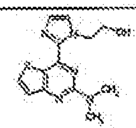
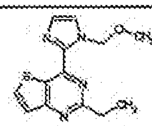
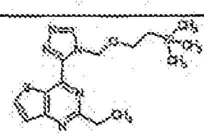
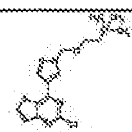
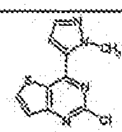
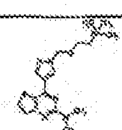
112 (E)		N-allyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine
113 (C)		2-isopropyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine
114 (C)		2-ethyl-4-(5-(4-methoxyphenyl)-2-oxazolyl)thieno[3,2-d]pyrimidine
115 (E)		N,N-dimethyl-4-(5-methyl-2-pyridyl)thieno[3,2-d]pyrimidine-2-amine
116 (G)		N-(4-(2-thiazolyl)thieno[3,2-d]pyrimidin-2-yl)acetamide
117 (A)		4-(2-furyl)-2-(2-thienylmethyl)thieno[3,2-d]pyrimidine
118 (A)		2-ethyl-4-(5-thiazolyl)thieno[3,2-d]pyrimidine
119 (A)		2-ethyl-4-(2-ethylthieno[3,2-d]pyrimidin-4-yl)thieno[3,2-d]pyrimidine
120 (D)		2-ethyl-4-(1H-triazol-3-yl)thieno[3,2-d]pyrimidine
121 (D)		2-ethyl-4-(1H-imidazol-2-yl)thieno[3,2-d]pyrimidine
122 (C)		4-(2-benzothiazolyl)-2-ethylthieno[3,2-d]pyrimidine
123 (E)		*tert*-butyl (2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)carbamate

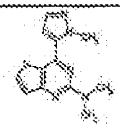
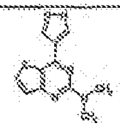
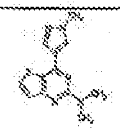
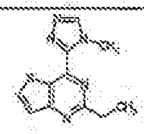
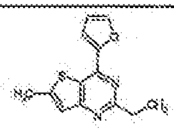
124 (F)		N-(2-aminoethyl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine
125 (H)		N-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)acetamide
126 (I)		N-ethyl-N'-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)urea
127 (I)		N-allyl-N'-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)urea
128 (I)		N-cyclohexyl-N'-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)urea
129 (H)		N-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)-3-methylbutanamide
130 (H)		methyl (2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)carbamate
131 (H)		isobutyl (2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)carbamate
132 (I)		N-*tert*-butyl-N'-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)urea
133 (I)		N-benzyl-N'-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)urea
134 (I)		N-phenyl-N'-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)urea
135 (I)		N-(4-chlorophenyl)-N'-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)urea

136 (I)		N-cyclohexyl-N'-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)thiourea
137 (I)		N-phenyl-N'-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)thiourea
138 (I)		N-(4-chlorophenyl)-N'-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)thiourea
139 (C)		2-*tert*-butyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine
140 (C)		2-cyclopropyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine
141 (C)		2-ethyl-4-(6-methyl-2-pyridyl)thieno[3,2-d]pyrimidine
142 (H)		N-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)cyclohexylcarboxamide
143 (H)		N-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)benzamide
144 (H)		4-chloro-N-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)benzamide
145 (H)		N-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)thiophene-2-carboxamide
146 (H)		phenyl (2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)carbamate
147 (H)		benzyl (2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)carbamate

148 (H)		N-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)methanesulphonamide
149 (H)		N-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)butanesulphonamide
150 (E)		(1RS)-N-(2-hydroxy-1-methylethyl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine
151 (E)		N-(3-(1H-imidazol-1-yl)propyl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine
152 (E)		(2S)-2-(2-hydroxymethylpyrrolidin-1-yl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine
153 (C)		4-(2-thiazolyl)-2-(2-thienyl)thieno[3,2-d]pyrimidine
154 (C)		2-(2-chloroethyl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine
155 (O)		4-(2-furyl)thieno[3,2-d]pyrimidine-2-carboxamide
156 (B)		2-chloro-4-(3-thienyl)thieno[3,2-d]pyrimidine
157 (E)		N,N-dimethyl-4-(3-thienyl)thieno[3,2-d]pyrimidine-2-amine
158 (B)		2-chloro-4-phenylthieno[3,2-d]pyrimidine
159 (E)		N,N-dimethyl-4-phenylthieno[3,2-d]pyrimidine-2-amine

160 (B)		2-chloro-4-(3-furyl)thieno[3,2-d]pyrimidine
161 (E)		N,N-dimethyl-4-(3-furyl)thieno[3,2-d]pyrimidine-2-amine
162 (A)		2-chloro-4-(2-furyl)-6-nitrothieno[3,2-d]pyrimidine
163 (B)		2-ethyl-4-(3-furyl)thieno[3,2-d]pyrimidine
164 (B)		4-(3,5-dimethyl-4-isoxazolyl)-2-ethylthieno[3,2-d]pyrimidine
165 (B)		2-chloro-4-(3-pyridyl)thieno[3,2-d]pyrimidine
166 (E)		N,N-dimethyl-4-(3-pyridyl)thieno[3,2-d]pyrimidine-2-amine
167 (C)		2-chloro-4-(1-methyl-1*H*-imidazol-2-yl)thieno[3,2-d]pyrimidine
168 (E)		N,N-dimethyl-4-(1-methyl-1*H*-imidazol-2-yl)thieno[3,2-d]pyrimidine-2-amine
169 (E)		N,N-dimethyl-4-(3-hydroxymethyl-2-furyl)thieno[3,2-d]pyrimidine-2-amine
170 (E)		N-(2-hydroxyethyl)-4-(1-methyl-1*H*-imidazol-2-yl)thieno[3,2-d]pyrimidine-2-amine
171 (E)		N-(2-hydroxyethyl)-4-(3-hydroxymethyl-2-furyl)thieno[3,2-d]pyrimidine-2-amine

172 (C)		2-chloro-4-(1-ethyl-1*H*-imidazol-2-yl)thieno[3,2-d]pyrimidine
173 (E)		N,N-dimethyl-4-(1-ethyl-1*H*-imidazol-2-yl)thieno[3,2-d]pyrimidine-2-amine
174 (E)		4-(1-ethyl-1*H*-imidazol-2-yl)-N-(2-hydroxyethyl)thieno[3,2-d]pyrimidine-2-amine
175 (C)		2-chloro-4-(1-(2-trimethylsilylethoxymethyl)-1*H*-imidazol-2-yl)thieno[3,2-d]pyrimidine
176 (E)		N,N-dimethyl-4-(1-(2-trimethylsilylethoxymethyl)-1*H*-imidazol-2-yl)thieno[3,2-d]pyrimidine-2-amine
177 (C)		N,N-dimethyl-4-((1-ethoxycarbonylmethyl)-1*H*-imidazol-2-yl)thieno[3,2-d]pyrimidine-2-amine
178 (K)		N,N-dimethyl-4-(1-(2-hydroxyethyl)-1*H*-imidazol-2-yl)thieno[3,2-d]pyrimidine-2-amine
179 (C)		2-ethyl-4-(1-methoxymethyl-1*H*-imidazol-2-yl)thieno[3,2-d]pyrimidine
180 (C)		2-ethyl-4-(4-(2-trimethylsilylethoxymethyl)-4*H*-1,2,4-triazol-3-yl)thieno[3,2-d]pyrimidine
181 (C)		2-chloro-4-(1-(2-trimethylsilylethoxymethyl)-1*H*-pyrazol-4-yl)thieno[3,2-d]pyrimidine
182 (C)		2-chloro-4-(1-methyl-1*H*-pyrazol-5-yl)thieno[3,2-d]pyrimidine
183 (E)		N,N-dimethyl-4-(1-(2-trimethylsilylethoxymethyl)-1*H*-pyrazol-4-yl)thieno[3,2-d]pyrimidine-2-amine

184 (E)		N,N-dimethyl-4-(1-methyl-1*H*-pyrazol-5-yl)thieno[3,2-d]pyrimidine-2-amine
185 (D)		N,N-dimethyl-4-(1*H*-pyrazol-4-yl)thieno[3,2-d]pyrimidine-2-amine
186 (C)		N,N-dimethyl-4-(1-methyl-1*H*-pyrazol-4-yl)thieno[3,2-d]pyrimidine-2-amine
187 (C)		2-ethyl-4-(4-methyl-4*H*-1,2,4-triazol-3-yl)thieno[3,2-d]pyrimidine
188 (A)		2-ethyl-4-(2-furyl)-6-methylthieno[3,2-d]pyrimidine

The general synthetic methods used for the preparation of these examples are set out below as Methods A to T.

Method A

2-Chloro-4-(2-furyl)thieno[3,2-d]pyrimidine (Example 3)

A solution of 2,4-dichlorothieno[3,2-d]pyrimidine (205 mg, 1 mmol) in DMF (4 mL) was treated with $PdCl_2(PPh_3)_2$ (35 mg, 0.05 mmol) and 2-(tributylstannyl)-furan (315 μL, 1 mmol), stirred at room temperature for 16 h, the reaction mixture purified directly by chromatography (SiO_2: EtOAc : Heptane, 1:9) and the resulting cream solid recrystallised (EtOAc/Heptane) to give the *title compound* (122 mg, 52 %) as a cream solid.

Method B

2-Chloro-4-(5-chloro-2-thienyl)thieno[3,2-d]pyrimidine

A solution of $Pd(OAc)_2$ (12 mg, 5 mol%) and PPh_3 (52 mg, 20 mol%) in THF (2 mL) was stirred for 5 min, treated dropwise with a solution of 2,4-dichlorothieno[3,2-d]pyrimidine (205 mg, 1 mmol) in THF (1 mL), stirred for 5 min, treated with 5-chlorothiophene-2-boronic acid (244mg, 1.5mmol) then saturated aqueous $NaHCO_3$ (1mL) refluxed for 4 h, cooled, diluted with H_2O and filtered to give the *title compound* (268 mg, 94 %) as a grey

solid; NMR δ_H (400 MHz, $CDCl_3$) 7.10 (1H, d, *J* 4.0 Hz), 7.55 (1H, d, *J* 5.5 Hz), 7.85 (1H, d, *J* 4.5 Hz) and 8.08 (1H, d, *J* 5.5 Hz)

Method C

2-Chloro-4-(2-thiazolyl)thieno[3,2-d]pyrimidine (Example 64)

A stirred solution of thiazole (0.14 mL, 2 mmol) in dry THF (10 mL) at −78 °C, under argon was treated with n-BuLi (1.6-M in hexanes, 1.3 mL, 2 mmol), stirred for 30 min, treated with a solution of $ZnCl_2$ (1.0-M in Et_2O, 2.0 mL, 2 mmol) and allowed to warm gradually to room temperature. The mixture was treated with a solution of 2,4-dichlorothieno[3,2-d]pyrimidine (205 mg, 1 mmol) in THF (5 mL) then $Pd(PPh_3)_4$ (100 mg, 10 mol%) refluxed for 17 h, cooled, diluted with saturated NH_4Cl solution and extracted with EtOAc. The organic extracts were dried ($MgSO_4$), concentrated *in vacuo* and purified by chromatography [SiO_2; isohexane:CH_2Cl_2 (2:1)] to give the *title compound* (75 mg, 26 %) as a white solid.

Method D

2-Ethyl-4-(1H-imidazol-2-yl)thieno[3,2-d]pyrimidine (Example 121)

A stirred solution of 1-(2-trimethylsilyl)ethoxymethyl-1*H*-imidazole (295 mg, 1.5 mmol) in dry THF (10 mL) at −78 °C, under argon was treated with n-BuLi (1.6-M in hexanes, 0.93 mL, 1.5 mmol), stirred for 30 min, treated with a solution of $ZnCl_2$ (1.0-M in Et_2O, 1.5 mL, 1.5 mmol) and the mixture allowed to warm gradually to room temperature. The mixture was treated with 4-chloro-2-ethylthieno[3,2-d]pyrimidine (148 mg, 0.75 mmol) and $Pd(PPh_3)_4$ (100 mg), refluxed for 3 h, cooled, diluted with saturated NH_4Cl solution, extracted with EtOAc, dried ($MgSO_4$), concentrated *in vacuo* and purified by chromatography [SiO_2; heptane : EtOAc (7:1) then (4:1)] to give the intermediate coupled product as a viscous oil (140 mg). A portion of this material (130 mg, 0.36 mmol) was dissolved in THF (5 mL), treated with a solution of tetra-*n*-butylammonium fluoride (1-M in THF, 0.72 mL, 0.72 mmol), refluxed for 4 hr, cooled, extracted with EtOAc, dried ($MgSO_4$) concentrated *in vacuo* and purified by chromatography [SiO_2; heptane : EtOAc (4:1) then (2:1)] to give the *title compound* (62 mg, 39 %) as a white solid.

Method E

7-Bromo-4-(2-furyl)-N-(2-hydroxyethyl)thieno[3,2-d]pyrimidine-2-amine (Example 15)

A solution of 7-bromo-2-chloro-4-(2-furyl)thieno[3,2-d]pyrimidine (110 mg, 0.35 mmol) in 1-methyl-2-pyrrolidinone (1 mL) was treated with ethanolamine (32 µL, 0.52 mmol), heated at 90 °C for 16h, cooled, poured into water, extracted with EtOAc, dried ($MgSO_4$), concentrated *in vacuo* and purified by chromatography (SiO_2: EtOAc : Heptane, 1:1) to give the *title compound* (45 mg, 38 %) as a yellow solid.

Method F

4-(2-Furyl)thieno[3,2-d]pyrimidine-2-amine (Example 79)

A solution of N-(3,4-dimethoxybenzyl)-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine (199 mg, 0.54 mmol) in TFA (1 mL) was heated at 60 °C for 1h, cooled, poured into sat. $NaHCO_3$, extracted with EtOAc, dried ($MgSO_4$), concentrated *in vacuo* and purified by chromatography (SiO_2: EtOAc : Heptane, 1:1 and MeOH : DCM, 1:19) to give the *title compound* (108 mg, 92 %) as a cream solid.

Method G

N-(4-(2-Furyl)thieno[3,2-d]pyrimidin-2-yl)acetamide (Example 101)

An ice-cold solution of 4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine (130 mg, 0.6 mmol) in pyridine (1 mL) was treated with acetyl chloride (47 µL, 0.66 mmol),stirred at room temperature for 16 h, poured into water, extracted with EtOAc, dried ($MgSO_4$) and concentrated *in vacuo* and purified by chromatography (SiO_2: EtOAc : Heptane, 1:1) to give the *title compound* (125 mg, 80 %) as a cream solid.

Method H

N-(2-(4-(2-Thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)acetamide (Example 125)

A solution of N-(2-aminoethyl)-4-(2-thiazolyl))thieno[3,2-d]pyrimidine-2-amine (0.040 g, 0.14 mmol) in DMF (2 mL) was treated with triethylammonium methylpolystyrene carbonate (0.066 g, 0.22 mmol) followed by acetyl chloride (0.023 g, 0.29 mmol), shaken at room temperature for 7 h, treated with tris-(2-aminoethyl)amine polystyrene (0.19 g, 0.87 mmol), shaken at room temperature for 16 h, treated with polystyrene 4-

benzyloxybenzaldehyde (0.19 g, 0.28 mmol), shaken for a further 3 h, filtered and concentrated *in vacuo* to give the *title compound* as a yellow solid.

Method I

N-Ethyl-N'-(2-(4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-ylamino)ethyl)urea (Example 126)

A solution of N-(2-aminoethyl)-4-(2-thiazolyl))thieno[3,2-d]pyrimidine-2-amine (0.040 g, 0.14 mmol) in anhydrous DMF (2 mL) was treated with ethyl isocyanate (0.015 g, 0.22 mmol), shaken at 35 °C for 1 h, treated with tris-(2-aminoethyl)amine polystyrene (0.19 g, 0.88 mmol), shaken at 35 °C for 4 h, filtered and concentrated *in vacuo* to give the *title compound* as a yellow solid.

Method J

7-Amino-N,N-dimethyl-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine (Example 51)

A solution of N,N-dimethyl-4-(2-furyl)-7-nitrothieno[3,2-d]pyrimidine (85 mg, 0.29 mmol) in MeOH (4 mL), under argon, was treated with a catalytic amount of Pd on carbon (10%), hydrogenated at room temperature for 1 h, filtered through celite, concentrated *in vacuo* and purified by chromatography (SiO_2: EtOAc : Heptane, 1:4) to give the *title compound* (62 mg, 82 %) as a brown solid.

Method K

2-(4-(2-Furyl)thieno[3,2-d]pyrimidin-2-yl)ethanol (Example 54)

A solution of ethyl 4-(2-furyl)thieno[3,2-d]pyrimidine-2-acetate (0.10 g, 0.35 mmol) in dichloromethane (13 mL) at –75 °C was treated dropwise with di-*iso*-butylaluminium hydride (0.87 mL, 1.0-M), stirred for 17 h, warmed to ambient temperature and partitioned between Rochelle's salt and dichloromethane. The combined organic phase was dried ($MgSO_4$), concentrated *in vacuo* and purified by chromatography (SiO_2: EtOAc) to give the *title compound* (21 mg, 25 %) as a white solid.

Method L

4-(2-Furyl)-2-vinylthieno[3,2-d]pyrimidine (Example 69)

A solution of 2-(4-(2-furyl)thieno[3,2-d]pyrimidin-2-yl)ethanol (0.15 g, 0.61 mmol) in THF (5 mL) at 0 °C was treated with diisopropylethylamine (0.095g, 0.73 mmol) then

methanesulfonyl chloride (0.72 g, 0.67 mmol), warmed to room temperature over 16 h, partitioned between ethyl acetate and water, the organic phase dried ($MgSO_4$) and concentrated *in vacuo* to give the intermediate mesylate (0.10 g, 50 %) as a white solid. A sample of this compound (59 mg, 0.18 mmol) was dissolved in CH_2Cl_2, treated with DBU (0.042 g, 0.27 mmol), stirred at room temperature for 18 h, partitioned between ethyl acetate and water and the organic phase was dried ($MgSO_4$) and concentrated *in vacuo* to give the *title compound* (22 mg, 50 %) as a white solid.

Method M

3-(4-(2-Furyl)thieno[3,2-d]pyrimidine-2-yl)propionic acid (Example 49)

A solution of ethyl 3-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-yl)propionate (0.07 g, 0.23 mmol) in THF (1.0 mL) and water (1.0 mL) was treated with lithium hydroxide (0.10 g, 2.32 mmol), stirred at room temperature for 16 h, concentrated *in vacuo*, dissolved in water, acidified to pH 2 by the addition of HCl (0.1 mL, 6.0-M), cooled in ice and filtered to give the *title compound* (0.052 g, 81 %) as a white solid.

Method N

4-(2-Furyl)-2-(3-oxo-3-(1-pyrrolidinyl)propyl)thieno[3,2-d]pyrimidine (Example 50)

A mixture of trimethylaluminium in toluene (1.3 mL, 2.0-M) and pyrrolidine (0.22 mL, 2.65 mmol) in toluene was heated at 80 °C for 0.5 h, treated with a solution of ethyl 3-(4-(2-furyl)thieno[3,2-d]pyrimidine-2-yl)propionate (0.1 g, 0.33 mmol) in toluene (2.0 mL), stirred at 80 °C for 17 h, cooled to room temperature and partitioned between sat. aq. NH_4Cl and ethyl acetate. The combined organic phase was dried ($MgSO_4$), concentrated *in vacuo* and purified by chromatography (SiO_2; EtOAc-methanol, 9:1) to give the *title compound* (27 mg, 25 %).

Method O

4-(2-Furyl)thieno[3,2-d]pyrimidine-2-carboxamide (Example 155)

Ammonia gas was bubbled through a hot solution of ethyl 4-(2-furyl)thieno[3,2-d]pyrimidine-2-carboxylate (0.156 g, 0.57 mmol) in ethanol (20 mL) for 3 h then the mixture cooled and the resulting white solid filtered to give the *title compound* (94 mg, 67 %)as a white solid.

Method P

4,7-Bis(2-furyl)-N,N-dimethylthieno[3,2-d]pyrimidine-2-amine (Example 31)

A mixture of $AsPh_3$ (73 mg, 0.24 mmol) in DMF (2 mL) was treated with $Pd(OAc)_4$ (13 mg, 0.06 mmol), stirred at room temperature for 10 min, treated with 7-bromo-N,N-dimethyl-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine (194 mg, 0.6 mmol) and 2-(tributylstannyl)-furan (340 μL, 1.1 mmol), heated to 100 °C for 16 h, cooled, poured into water, extracted with EtOAc, dried ($MgSO_4$), concentrated *in vacuo* and purified by chromatography (SiO_2: EtOAc : Heptane, 1:9) to give the *title compound* (27 mg, 15 %) as a orange solid.

Method Q

2-Isopropylthieno[3,2-d]pyrimidine-4-ol

A mixture of 3-aminothiophene-2-carboxamide (2.0 g, 14.1 mmol) and triethylamine (1.71 g, 16.9 mmol) in toluene (20 mL) at room temperature was treated with 2-methylpropionic anhydride (2.45 g, 15.5 mmol), refluxed for 4 h, cooled, poured into saturated $NaHCO_3$ (100 mL) and extracted with ethyl acetate (4 x 50 mL). The combined organic phase was washed with brine(2 x50 mL), dried (Na_2SO_4) and concentrated in vacuo to the intermediate *N*-acylated compound (2.90 g, 99 %)as a pale yellow solid. A sample of this compound (2.85 g, 13.44 mmol) was dissolved in NaOH (34 mL, 1.0-M), refluxed for 1 h, cooled, acidified to pH 2 by addition of HCl (7.0 mL, 6.0-M), filtered and dried to give the *title compound* (2.30 g, 88 %) as a white solid: IR ν_{max} (Nujol)/cm^{-1} 2956, 2925, 1676, 1599, 1464, 780; NMR δ_H (400 MHz, DMSO) 1.20 (6H, d *J* 6.5 Hz), 2.90 (1H, heptet, *J* 6.5 Hz), 7.40 (1H, d *J* 5.0 Hz), 8.15 (1H, d, *J* 5.0 Hz) and 12.30 (1H, br).

Method R

2-Cyclopropylthieno[3,2-d]pyrimidine-4-ol

Dry HCl gas was bubbled through a solution of methyl 3-aminothiophene-2-carboxylate (1.64 g, 10.4 mmol) and cyclopropanecarbonitrile (27 mL) in dioxane (40 mL) for 1 h then the reaction mixture was diluted with cold water (2 volumes), basified with NH_4OH (50 mL) and the resulting solid filtered and air dried to give the *title compound* (1.44 g, 72 %) as a white solid: IR ν_{max} (Nujol)/cm^{-1} 2925, 1664, 1597, 788; NMR δ_H (400 MHz, DMSO) 1.04 (4H, m), 2.00 (1H, m), 7.20 (1H, d *J* 5.0 Hz), 8.10 (1H, d, *J* 5.0 Hz) and 12.60 (1H, br).

Method S

4-Chloro-2-isopropylthieno[3,2-d]pyrimidine

A suspension of 2-isopropylthieno[3,2-d]pyrimidine-4-ol (1.66 g, 8.56 mmol) in $POCl_3$ (30 mL) was refluxed for 1 h, cooled, diluted with chloroform (100 mL) and poured into a mixture of ice and NH_4OH (150 mL). The organic phase was separated, washed with saturated $NaHCO_3$ (20 mL), water and brine, dried ($MgSO_4$) and concentrated *in vacuo* to give the *title compound* (2.01 g, 99 %) as a pale yellow solid: IR ν_{max} (Nujol)/cm^{-1} 3065, 2960, 2926, 2855, 1561, 1513, 1457, 803; NMR δ_H (400 MHz, $CDCl_3$) 1.40 (6H, d *J* 6.5 Hz), 3.38 (1H, heptet, *J* 6.5 Hz), 7.60 (1H, d *J* 5.0 Hz), 8.05 (1H, d, *J* 5.0 Hz).

Method T

Ethyl 4-hydroxythieno[3,2-d]pyrimidine-2-carboxylate

A mixture of 3-aminothiophene-2-carboxamide (1.23 g, 8.65 mmol) and EtOH (25 mL) was treated with NaOEt (1.2 g, 17.3 mmol) and diethyloxalate (2.3 mL, 17.3 mmol), refluxed for 18 h, cooled, concentrated *in vacuo*, treated with water, acidified with HOAc and filtered to give the *title compound* (1.43 g, 74 %) as a cream solid: IR ν_{max} Nujol)/cm^{-1} 3180, 3119, 3078, 3006, 2955, 2924, 2854, 1737, 1667, 1651, 1300 and 1176; NMR δ_H (400 MHz, DMSO) 1.37 (3H, t, *J* 7.0 Hz), 4.40 (2H, q, *J* 7.0 Hz), 7.58 (1H, d, *J* 5.0 Hz), 8.30 (1H, d, *J* 5.1 Hz), and 12.92 (1H, s).

Table 2 – Analytical data

HPLC is carried out using the following conditions: Column, Supelcosil ABZ$^+$ (170 x 4.6 mm), particle size 5 µM, mobile phase MeOH : 10 mM aq NH_4OAc (80:20), (70:30) or (60:40) (specified in Table 2), flow rate 1.0 mL/min., detection wavelength λ = 230 nM (unless otherwise stated), retention times are provided in Table 2.

Example	Yield(%)	Physical Data
1	61	Mp 135.6 – 135.8 °C; IR ν_{max} (Nujol)/cm^{-1} 3111, 3082, 3072, 1529, 1467, 1425, 1254, 1238 and 1205; NMR δ_H (400 MHz, $CDCl_3$) 7.28 (1H, dd, *J* 5.0, 4.0 Hz), 7.54 (1H, d, *J* 5.5 Hz), 7.69 (1H, dd, *J* 5.0, 1.0 Hz), 8.07 (1H, d, *J* 5.5 Hz), 8.08 (1H, dd, *J* 4.0, 1.0 Hz); Anal. Calcd for

		$C_{10}H_5ClN_2S_2$: C, 47.52; H, 1.99, N, 11.08. Found: C, 47.54; H, 2.00; N, 10.93; M/Z 253 $(M+H)^+$.
2	98	mp 139.2 – 140.0 °C; IR ν_{max} (Nujol)/cm^{-1} 1551, 1517, 1466, 1393, 1361, 793 and 707; NMR δ_H (400 MHz, $CDCl_3$) 3.30 (6H, s), 7.22 (1H, dd, *J* 5.0, 4.0 Hz), 7.27 (1H, d, *J* 5.5 Hz), 7.54 (1H, dd, *J* 5.5, 1.0 Hz), 7.79 (1H, d, *J* 5.5 Hz), 7.95 (1H, dd, *J* 3.5, 1.0 Hz); Anal. Calcd for $C_{12}H_{11}N_3S_2$: C, 55.15; H, 4.24, N, 16.07. Found: C, 55.05; H, 4.12; N, 15.88.
3	52	mp 146.9 – 147.6 °C; IR ν_{max} (Nujol)/cm^{-1} 3132, 3105, 3064, 1594, 1522, 1463 and 1264; NMR δ_H (400 MHz, $CDCl_3$) 6.69 – 6.72 (1H, m), 5.50 (1H, d, *J* 5.5 Hz), 7.60 (1H, dd, *J* 3.5, 1.0 Hz), 7.80 (1H, d, *J* 1.0 Hz), 8.10 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{10}H_5ClN_2OS + 0.4\ H_2O$: C, 49.25; H, 2.40, N, 11.49. Found: C, 48.87; H, 2.04; N, 11.65.
4	78	mp 128.5 – 128.9 °C; IR ν_{max} (Nujol)/cm^{-1} 3314, 3065, 1542, 1498, 1466 and 1363; NMR δ_H (400 MHz, $CDCl_3$) 1.71 – 1.81 (1H, m), 1.88 – 2.08 (2H, m), 2.13 – 2.23 (1H, m), 3.68 – 3.79 (3H, m), 3.82 – 3.98 (2H, m), 4.40 (1H, s), 7.21 – 7.27 (2H, m), 7.56 (1H, dd, *J* 5.0, 1.0 Hz), 7.83 (1H, d, *J* 5.5 Hz), 7.98 (1H, dd, *J* 4.0, 1.0 Hz); Anal. Calcd for $C_{15}H_{15}N_3OS_2$: C, 56.76; H, 4.76, N, 13.23. Found: C, 56.72; H, 4.80; N, 13.14.
5	77	mp 129.3 – 130.4 °C; IR ν_{max} (Nujol)/cm^{-1} 3125, 3095, 3066, 1601, 1554, 1462, 1403 and 792; NMR δ_H (400 MHz, $CDCl_3$) 3.29 (6H, s), 6.60 – 6.64 (1H, m), 7.23 (1H, d, *J* 5.5 Hz), 7.38 (1H, d, *J* 3.5 Hz), 7.70 – 7.72 (1H, m), 7.80 – 7.84 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{12}H_{11}N_3OS$: C, 58.76; H, 4.52, N, 17.12. Found: C, 58.89; H, 4.52; N, 16.89.
6	75	mp dec. >230 °C; IR ν_{max} (Nujol)/cm^{-1} 3426, 3160, 3075, 1616, 1573, 1523 and 1447; NMR δ_H (400 MHz, DMSO) 2.13 – 2.22 (2H, m), 3.45 (2H, t, *J* 6.5 Hz), 4.33 (2H, t, *J* 7.0 Hz), 4.49 – 4.87 (1H, s), 7.36 – 7.39 (1H, m), 7.43 – 7.46 (1H, m), 7.69 – 7.72 (1H, m), 7.84 – 7.87 (1H, m), 8.00 (1H, d, *J* 4.5 Hz), 8.04 (1H, d, *J* 4.0 Hz), 8.42 (1H, d, *J* 5.5 Hz), 9.23 (1H, s); Anal. Calcd for $C_{16}H_{15}N_5S_2 + 2HCl + 0.25\ H_2O$: C, 44.44, H, 4.43, N, 16.20. Found: C, 44.09; H, 4.34; N, 16.14.

7	61	mp 110.6 – 111.8 °C; IR ν_{max} (Nujol)/cm^{-1} 3266, 1590, 1553, 1516, 1461 and 791; NMR δ_H (400 MHz, $CDCl_3$) 3.67 – 3.73 (2H, m), 3.89 – 3.93 (2H, m), 3.93 – 4.08 (1H, s), 5.56 (1H, t, *J* 5.0 Hz), 7.21 – 7.25 (2H, m), 7.56 (1H, dd, *J* 5.0, 1.0 Hz), 7.83 (1H, d, *J* 5.5 Hz), 7.97 (1H, dd, *J* 3.5, 1.0 Hz); Anal. Calcd for $C_{12}H_{11}N_3OS_2$: C, 51.97, H, 4.00, N, 15.14. Found: C, 51.75; H, 3.96; N, 15.11.
8	95	mp 114.6 – 115.1 °C; IR ν_{max} (Nujol)/cm^{-1} 3412, 3059, 1549, 1481, 1464, 1341, 1327 and 725; NMR δ_H (400 MHz, $CDCl_3$) 4.13 (3H, s), 7.24 – 7.27 (1H, m), 7.42 (1H, d, *J* 5.5 Hz), 7.62 (1H, dd, *J* 5.0, 1.0 Hz), 7.96 (1H, d, *J* 5.5 Hz), 8.04 (1H, dd, *J* 3.5, 1.0 Hz); Anal. Calcd for $C_{11}H_8N_2OS_2$: C, 53.21, H, 3.25, N, 11.28. Found: C, 53.21; H, 3.27; N, 11.24.
9	36	IR ν_{max} (Nujol)/cm^{-1} 3065, 2925, 2855, 1539, 1464, 1352, 716; NMR δ_H (400 MHz, $CDCl_3$) 1.50 (3H, t *J* 7.5 Hz), 3.10 (2H, q, *J* 7.5 Hz), 7.26 (1H, m), 7.54 (1H, d, *J* 5.5 Hz), 7.61 (1H, dd, *J* 1.0, 5.0 Hz), 7.96 (1H, d, *J* 5.5 Hz), 8.04 (1H, dd, *J* 1.0, 3.8 Hz).
10	57	mp dec. >235 °C; IR ν_{max} (Nujol)/cm^{-1} 3417, 3105, 2623, 1654, 1633, 1508 and 1466; NMR δ_H (400 MHz, DMSO) 2.13 – 2.22 (2H, m), 3.49 (2H, t, *J* 6.5 Hz), 4.33 (2H, t, *J* 7.0 Hz), 4.02 – 4.66 (2H, s), 6.88 – 6.90 (1H, m), 7.45 (1H, s), 7.51 (1H, s), 7.70 (1H, t, *J* 1.7 Hz), 7.85 (1H, t, *J* 1.7 Hz), 8.23 (1H, s), 8.45 (1H, d, *J* 5.0 Hz), 9.22 (1H, s), 14.59 – 14.87 (1H, s); Anal. Calcd for $C_{16}H_{15}N_5OS$ + 2HCl + 1.5 H_2O: C, 45.18, H, 4.74, N, 16.47, Cl, 16.67. Found: C, 45.40; H, 4.39; N, 16.59, Cl, 16.42.
11	82	mp 147.6 – 148.8 °C; ; IR ν_{max} (Nujol)/cm^{-1} 3141, 3112, 3074, 1594, 1536, 1524, 1487, 1471, 1239, 1192, 1167, 1131 and 810; NMR δ_H (400 MHz, $CDCl_3$) 6.71 – 6.73 (1H, m), 7.66 (1H, dd, *J* 3.5, 1.0 Hz), 7.69 (1H, d, *J* 5.5 Hz), 7.81 – 7.83 (1H, m), 8.19 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{11}H_5F_3N_2OS$: C, 48.89, H, 1.86, N, 10.36. Found: C, 48.67; H, 1.92; N, 10.25.
12	78	mp 164.4 – 164.9 °C; IR ν_{max} (Nujol)/cm^{-1} 3153, 3121, 1596, 1498, 1466, 1272 and 804; NMR δ_H (400 MHz, $CDCl_3$) 2.51 (3H, s), 6.68 – 6.70 (1H, m), 7.57 (1H, dd, *J* 3.5, 1.0 Hz), 7.72 (1H, dd, *J* 2.5, 1.0 Hz),

		7.78 – 7.79 (1H, m); Anal. Calcd for $C_{11}H_7ClN_2OS$: C, 52.70, H, 2.82, N, 11.17. Found: C, 52.91; H, 2.82; N, 11.05.
13	34	mp dec. 213.9 °C; IR ν_{max} (Nujol)/cm^{-1} 3142, 3113, 3898, 3070, 1594, 1515, 1460, 1271 and 765; NMR δ_H (400 MHz, DMSO) 6.90 – 6.93 (1H, m), 7.68 (1H, d, *J* 3.5 Hz), 8.27 (1H, s), 8.83 (1H, s); Anal. Calcd for $C_{10}H_4BrClN_2OS$: C, 38.06, H, 1.28, N, 8.87. Found: C, 38.22; H, 1.38; N, 8.74.
14	75	mp 107.9 – 108.9 °C; IR ν_{max} (Nujol)/cm^{-1} 3279, 1607, 1572, 1460, 1377, 1067 and 791; NMR δ_H (400 MHz, $CDCl_3$) 3.66 – 3.72 (2H, m), 3.88 – 3.93 (2H, m), 4.33 – 4.60 (1H, s), 5.56 (1H, t, *J* 5.0 Hz), 6.62 – 6.65 (1H, m), 7.21 (1H, d, *J* 5.5 Hz), 7.38 (1H, d, *J* 3.5 Hz), 7.73 (1H, s), 7.88 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{12}H_{11}N_3O_2S$: C, 55.16, H, 4.24, N, 16.07. Found: C, 55.16; H, 4.23; N, 15.97.
15	38	mp 173.4 – 174.4 °C; IR ν_{max} (Nujol)/cm^{-1} 3394, 3260, 3110, 3083, 1600, 1555, 1463 and 1439; NMR δ_H (400 MHz, $CDCl_3$) 3.70 – 3.72 (2H, m), 3.89 – 3.95 (2H, m), 4.47 – 4.67 (1H, s), 5.67 – 5.74 (1H, m), 6.64 – 6.67 (1H, m), 7.40 (1H, d, *J* 3.5 Hz), 7.74 (1H, s), 7.87 (1H, s); Anal. Calcd for $C_{12}H_{10}BrN_3O_2S + 0.25\ H_2O$: C, 41.27; H, 3.18, N, 12.03. Found: C, 41.28; H, 3.04; N, 12.04.
16	75	mp 149.9 – 150.6 °C; IR ν_{max} (Nujol)/cm^{-1} 3404, 3219, 1602, 1550, 1507, 1464 and 1440; NMR δ_H (400 MHz, $CDCl_3$) 2.38 (3H, s), 3.67 – 3.73 (2H, m), 3.88 – 3.94 (2H, m), 5.13 (1H, s), 5.57 (1H, t, *J* 5.0 Hz), 6.62 – 6.64 (1H, m), 7.37 (1H, dd, *J* 3.5, 1.0 Hz), 7.51 (1H, d, *J* 1.0 Hz), 7.72 – 7.73 (1H, m); Anal. Calcd for $C_{13}H_{13}N_3O_2S$: C, 56.71; H, 4.76, N, 15.25. Found: C, 56.67; H, 4.79; N, 15.19.
17	64	mp 231.0 – 231.6 °C; IR ν_{max} (Nujol)/cm^{-1} 3109, 3094, 1531, 1469, 1232 and 790; NMR δ_H (400 MHz, DMSO) 7.48 – 7.58 (2H, m), 7.72 (1H, d, *J* 5.5 Hz), 8.10 – 8.17 (2H, m), 8.52 (1H, s), 8.75 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{14}H_7ClN_2S_2$: C, 55.33; H, 2.33, N, 9.25. Found: C, 55.22; H, 2.32; N, 9.41.

18	56	IR ν_{max} (Nujol)/cm^{-1} 3096, 2924, 1595, 1528, 1488, 1463, 1303, 1016, 808 and 768; NMR δ_H (400 MHz, DMSO) 1.36 (3H, t, *J* 7.7 Hz), 3.00 (2H, q, *J* 7.7 Hz), 6.85 (1H, dd, *J* 1.8, 3.5 Hz), 7.54 (1H, dd, *J* 0.8, 3.5 Hz), 7.58 (1H, d, *J* 5.5 Hz), 8.17 (1H, dd, *J* 0.8, 1.8 Hz), 8.49 (1H, d, *J* 5.5 Hz).
19	89	mp 166.5 – 167.3 °C; IR ν_{max} (Nujol)/cm^{-1} 3094, 3053, 1556, 1463, 1407, 1354 and 793; NMR δ_H (400 MHz, $CDCl_3$) 3.33 (6H, s), 7.29 (1H, d, *J* 5.5 Hz), 7.37 – 7.43 (2H, m), 7.82 (1H, d, *J* 5.5 Hz), 7.87 – 7.92 (2H, m), 8.16 (1H, s); Anal. Calcd for $C_{16}H_{13}N_3S_2$: C, 61.71; H, 4.21, N, 13.49. Found: C, 61.82; H, 4.26; N, 13.52.
20	64	mp 173.4 – 174.4 °C; IR ν_{max} (Nujol)/cm^{-1} 3409, 3260, 3126, 3094, 1587, 1545 and 1339; NMR δ_H (400 MHz, $CDCl_3$) 3.70 – 3.77 (2H, m), 3.90 – 3.97 (2H, m), 5.60 (1H, t, *J* 5.0 Hz), 7.27 (1H, d, *J* 5.5 Hz), 7.39 – 7.46 (2H, m), 7.86 – 7.93 (3H, m), 8.19 (1H, s); Anal. Calcd for $C_{16}H_{13}N_3OS_2$ + 0.25 H_2O: C, 57.93; H, 4.10, N, 12.66. Found: C, 57.78; H, 3.96; N, 12.76.
21	42	mp 112.3 – 122.7 °C; NMR δ_H (400 MHz, $CDCl_3$) 1.30 (3H, t, *J* 7.3 Hz), 3.54 – 3.62 (2H, m), 5.06 (1H, s), 7.26 (1H, d, *J* 5.5 Hz), 7.45 – 7.48 (1H, m), 7.81 (1H, d, *J* 5.5 Hz), 7.90 (1H, dd, *J* 5.0 Hz), 8.20 – 8.23 (1H, m); Anal. Calcd for $C_{12}H_{11}N_3S_2$: C, 55.15; H, 4.24, N, 16.07. Found: C, 55.13; H, 4.29; N, 15.90.
22	63	mp 118.7 – 119.5 °C; IR ν_{max} (Nujol)/cm^{-1} 3094, 1602, 1552, 1464 and 1377; NMR δ_H (400 MHz, $CDCl_3$) 3.33 (6H, s), 6.61 – 6.64 (1H, m), 7.40 (1H, d, *J* 3.5 Hz), 7.71 – 7.72 (1H, m), 7.81 (1H, s); Anal. Calcd for $C_{12}H_{10}BrN_3OS$: C, 44.46; H, 3.11, N, 12.96. Found: C, 44.24; H, 3.06; N, 13.01.
23	90	mp 113.1 – 113.7 °C; IR ν_{max} (Nujol)/cm^{-1} 3115, 1602, 1560, 1548, 1508, 1466 and 1409; NMR δ_H (400 MHz, $CDCl_3$) 2.38 (3H, s), 3.31 (6H, s), 6.58 – 6.62 (1H, m), 7.36 (1H, d, *J* 3.5 Hz), 7.44 – 7.45 (1H, m), 7.69 – 7.70 (1H, m); Anal. Calcd for $C_{16}H_{13}N_3OS$ + 0.15 H_2O: C, 59.59; H, 5.12, N, 16.04. Found: C, 59.83; H, 2.89; N, 15.70.

24	31	mp 209.2 – 209.5 °C; IR ν_{max} (Nujol)/cm^{-1} 1531, 1523, 1463, 1377, 1247 and 781; NMR δ_H (400 MHz, $CDCl_3$) 7.47 (1H, m), 7.54 (1H, d, *J* 6.0 Hz), 7.95 (1H, dt, *J* 8.0, 2.0 Hz), 8.19 (1H, d, *J* 5.5 Hz), 8.73 – 8.77 (1H, m), 8.84 – 8.87 (1H, m); Anal. Calcd for $C_{11}H_6ClN_3S$ + 0.1 H_2O: C, 52.56; H, 2.45, N, 16.72. Found: C, 52.69; H, 2.41; N, 16.64.
25		IR ν_{max} (Nujol)/cm^{-1} 2955, 2924, 2854, 1600, 1555, 1526, 1490, 1456, 1378 and 1270; NMR δ_H (400 MHz, DMSO) 8.18 (1H, m) 7.97 (1H, s), 7.35 (1H, m), 7.14 (1H, m), 6.67 (1H, m), 3.68 – 3.58 (4H, m), 3.58 – 3.48 (4H, m).
26		IR ν_{max} (Nujol)/cm^{-1} 3261, 2924, 2854, 1604, 1573, 1547, 1513, 1455, 1443 and 1330; NMR δ_H (400 MHz, $CDCl_3$) 7.86 (1H, d, *J* 5.5 Hz), 7.72 (1H, s), 7.48 – 7.23 (7H, m), 6.62 (1H, dd, *J* 4.0, 1.5 Hz), 5.53 (1H, br s), 4.76 (2H, d, *J* 5.9 Hz).
27	13	mp 186.6 – 188.0 °C; IR ν_{max} (Nujol)/cm^{-1} 3053, 1556, 1466, 1359 and 786; NMR δ_H (400 MHz, $CDCl_3$) 3.37 (6H, s), 7.27 – 7.33 (1H, m), 7.39 – 7.45 (1H, m), 7.86 – 7.95 (2H, m), 8.66 (1H, d, *J* 8.0 Hz), 8.81 – 8.84 (1H, m).
28	40	mp 197.1 - 197.7 °C; IR ν_{max} (Nujol)/cm^{-1} 3406, 3103, 3084, 1569, 1520 and 1464; NMR δ_H (400 MHz, $CDCl_3$) 6.49 – 6.50 (1H, m), 7.14 (1H, dt, *J* 3.0, 1.0 Hz), 7.20 – 7.23 (1H, m), 7.48 (1H, d, *J* 5.5 Hz), 8.01 (1H, d, *J* 5.5 Hz), 9.88 – 10.01 (1H, s); Anal. Calcd for $C_{10}H_6ClN_3S$: C, 50.96; H, 2.57, N, 17.82. Found: C, 50.87; H, 2.54; N, 17.64.
29	31	IR ν_{max} (Nujol)/cm^{-1} 2924, 2854, 1739, 1727, 1598, 1532, 1467, 1369, 1348 and 1191; NMR δ_H (400 MHz, $CDCl_3$) 8.05 (1H, m), 7.78 (1H, m), 7.60 (1H, m), 7.49 (1H, m), 6.42 (1H, m), 4.20 (2H, q, J 7.0 Hz), 4.18 (2H, s) and 1.22 (3H, t, J 7.0 Hz); M/Z 289 $(M+H)^+$.
30	67	mp 183.2 – 183.8 °C; IR ν_{max} (Nujol)/cm^{-1} 3071, 1536, 1522, 1465 and 1252; NMR δ_H (400 MHz, $CDCl_3$) 7.58 (1H, d, *J* 5.5 Hz), 8.23 (1H, d, *J* 5.5 Hz), 8.79 – 8.83 (2H, m), 9.95 (1H, d, *J* 1.5 Hz); Anal. Calcd for $C_{10}H_5ClN_4S$: C, 48.30; H, 2.03, N, 22.52. Found: C, 48.28; H, 2.10; N, 22.40.

31	15	IR ν_{max} (Nujol)/cm^{-1} 2726, 1561, 1509, 1461 and 1377; NMR δ_H (400 MHz, $CDCl_3$) 3.35 (6H, s), 6.54 – 6.55 (1H, m), 6.62 – 6.64 (1H, m), 7.41 (1H, dd, *J* 3.5, 1.0 Hz), 7.45 (1H, d, *J* 3.5 Hz), 7.48 – 7.49 (1H, m), 7.72 – 7.73 (1H, m), 8.05 (1H, s); Anal. Calcd for $C_{16}H_{13}N_3O_2S$ + 0.3 H_2O: C, 60.67; H, 4.33, N, 13.27. Found: C, 60.49; H, 4.09; N, 13.33.
32	94	mp 247.4 – 248.6 °C; IR ν_{max} (Nujol)/cm^{-1} 3080, 3072, 1568, 1544, 1462 and 1402; NMR δ_H (400 MHz, $CDCl_3$) 3.29 (6H, s), 6.41 – 6.44 (1H, m), 7.04 – 7.06 (1H,m), 7.09 – 7.12 (1H, m), 7.23 (1H, d, *J* 5.5 Hz), 7.76 (1H, d, *J* 5.0 Hz), 9.74 – 9.83 (1H, s); Anal. Calcd for $C_{12}H_{12}N_4S$ + 0.2 H_2O: C, 58.14; H, 5.04, N, 22.60. Found: C, 58.16; H, 4.84; N, 22.64.
33	100	mp 173.9 – 174.3 °C; IR ν_{max} (Nujol)/cm^{-1} 1586, 1558, 1531, 1462, 1352 and 793; NMR δ_H (400 MHz, $CDCl_3$) 3.36 (6H, s), 7.29 (1H, d, *J* 5.5 Hz), 7.92 (1H, d, *J* 5.5 Hz), 8.70 (1H, d, *J* 2.5 Hz), 8.76 – 8.78 (1H, m), 8.76 – 8.78 (1H, m), 9.87 (1H, d, *J* 1.5 Hz); Anal. Calcd for $C_{12}H_{11}N_5S$ + 0.1 H_2O: C, 55.62; H, 4.36, N, 27.03. Found: C, 55.46; H, 4.25; N, 26.83.
34	55	mp 191.5 – 192.4 °C; IR ν_{max} (Nujol)/cm^{-1} 3298, 3082, 3060, 1589, 1567, 1533, 1465, 1344, 1062 and 797; NMR δ_H (400 MHz, DMSO) 3.47 – 3.56 (2H, m), 3.57 – 3.65 (2H, m), 4.73 (1H, s), 7.19 (1H, s), 7.28 (1H, d, *J* 5.0 Hz), 8.31 (1H, d, *J* 5.5 Hz), 8.86 (1H, d, *J* 2.5 Hz), 8.91 (1H, dd, *J* 2.5, 1.5 Hz), 9.72 (1H, s).
35		IR ν_{max} (Nujol)/cm^{-1} 3140, 3089, 2925, 2854, 1601, 1552, 1527, 1519, 1493, 1455 and 1265; NMR δ_H (400 MHz, $CDCl_3$) 7.85 (1H, d, *J* 5.5 Hz), 7.72 (1H, s), 7.38 (1H, m), 7.22 (1H, d, *J* 5.5 Hz), 6.65 (1H, m), 4.05 – 3.91 (4H, m), 2.68 – 2.53 (4H, m), 2.41 (3H, s).
36		IR ν_{max} (Nujol)/cm^{-1} 3107, 3080, 2963, 2927, 2865, 1596, 1525, 1484, 1463, 1272 and 1236; NMR δ_H (400 MHz, $CDCl_3$) 7.97 (1H, d, *J* 5.5 Hz), 7.77 (1H, s), 7.48 (1H, m), 7.39 (1H, d, *J* 5.5 Hz), 6.67 (1H, m), 4.13 (1H, sept, *J* 7.0 Hz), 1.52 (3H, *J* 7.0 Hz).
37	95	mp 207 - 208 °C; IR ν_{max} (Nujol)/cm^{-1} 3073, 2956, 1592, 1513, 1462 1263, 1012, 794 and 768; NMR δ_H (400 MHz, $CDCl_3$) 1.47 (3H, t, *J* 7.5 Hz), 3.28 (2H, q, *J* 7.5 Hz), 6.66 (1H, dd, *J* 3.5, 1.5 Hz), 7.49 (1H, d, *J* 5.5 Hz), 7.74 - 7.79 (1H, m) and 7.97 (1H, d, *J* 5.5 Hz)

38	75	mp 109 - 110 °C; IR ν_{max} (Nujol)/cm^{-1} 3314, 2927, 1598, 1551, 1379, 1346, 1078, 795 and 744; NMR δ_H (400 MHz, $CDCl_3$) 1.60 - 1.80 (2H, m), 1.86 - 2.07 (2H, m), 2.14 - 2.26 (1H, m), 3.64 - 3.99 (4H, m), 4.38 (1H, m), 6.61 - 6.66 (2H, m), 7.22 - 7.28 (1H, m), 7.41 (1H, d, *J* 3.5 Hz), 7.74 (1H, d, *J* 2.5 Hz) and 7.88 (1H, d, *J* 5.5 Hz)
39	66	IR ν_{max} (Nujol)/cm^{-1} 3058, 22925, 1595, 1524, 1462, 1268 and 794; NMR δ_H (400 MHz, $CDCl_3$) 2.69 (3H, s), 6.66 (1H, dd, *J* 4.0, 2.0 Hz), 7.42 (1H, d, *J* 5.5 Hz), 7.51 (1H, d, *J* 3.5 Hz), 7.76 (1H, d, *J* 2.5 Hz) and 7.98 (1H, d, *J* 5.5 Hz)
40	73	mp 101-102 °C; IR ν_{max} (Nujol)/cm^{-1} 3255, 2925, 1610, 1550, 1515, 1446, 1331, 907 and 793; NMR δ_H (400 MHz, $CDCl_3$) 4.16 - 4.23 (2H, m), 5.16 (1H, dq, *J* 10.0, 1.5 Hz), 5.21 - 5.29 (1H, m); 5.32 (1H, dq, *J* 17.0, 1.5 Hz), 5.97 - 6.09 (1H, m), 6.63 (1H, dd, *J* 3.5, 2.0 Hz), 7.25 (1H, d, *J* 5.5 Hz), 7.39 (1H, d, *J* 3.5 Hz), 7.73 (1H, dd, *J* 2.5, 1.0 Hz) and 7.86 (1H, d, *J* 5.5 Hz)
41	56	mp 220.5 – 221.0 °C; IR ν_{max} (Nujol)/cm^{-1} 3135, 3082, 3080, 1594, 1544, 1519, 1505, 1463, 1341, 1265, 867, 782 and 750; NMR δ_H (400 MHz, DMSO) 6.94 – 6.96 (1H, m), 7.75 (1H, dd, *J* 3.5, 1.0 Hz), 8.33 (1H, d, *J* 1.0 Hz), 9.79 (1H, s); Anal. Calcd for $C_{10}H_4ClN_5O_3S_2O$: C, 42.64; H, 1.43, N, 14.91. Found: C, 42.94; H, 1.81; N, 15.05.
42		IR ν_{max} (Nujol)/cm^{-1} 3261, 2925, 2854, 1608, 1599, 1549, 1516, 1458, 1377 and 1329. NMR δ_H (400 MHz, $CDCl_3$) 7.86 (1H, d, *J* 5.5 Hz), 7.72 (1H, s), 7.38 (1H, m), 7.25 (1H, d, *J* 5.5 Hz), 7.65 (1H, m), 5.16 (1H, br s), 5.59 (2H, q, *J* 8.5 Hz), 1.32 (3H, t, *J* 8.5 Hz).
43		IR ν_{max} (Nujol)/cm^{-1} 2956, 2925, 2855, 1598, 1547, 1521, 1508, 1478, 1458 and 1349; NMR δ_H (400 MHz, $CDCl_3$) 7.80 (1H, m), 7.72 (1H, m), 7.39 (1H, m), 7.22 (1H, m), 6.62 (1H, m), 3.68 (4H, m) and 2.02 (4H, m).
44	21	mp 182.8 – 183.8 °C; IR ν_{max} (Nujol)/cm^{-1} 3152, 3128, 3107, 1601, 1558, 1543, 1498, 1477, 1406, 1321, 765 and 756; NMR δ_H (400 MHz, $CDCl_3$) 3.35 (6H, s), 6.65 – 6.67 (1H, m), 7.45 (1H, d, *J* 3.5 Hz), 7.74 – 7.75 (1H, m), 8.88 (1H, s); Anal. Calcd for $C_{12}H_{10}N_4O_3S$: C, 49.65; H, 3.47, N, 19.29. Found: C, 49.27; H, 3.49; N, 19.04.

45		IR ν_{max} (Nujol)/cm^{-1} 3250, 3084, 2924, 2854, 1608, 1580, 1548, 1515, 1485, 1443 and 1330; NMR δ_H (400 MHz, $CDCl_3$) 8.59 (1H, m), 7.88 (1H, m), 7.72 (1H, m), 7.66 (1H, m), 7.41 – 7.38 (1H, m), 7.25 (1H, m), 7.18 (1H, m), 6.63 (1H, m), 6.21 (1H, br s) and 4.89 (2H, d, *J* 5.6 Hz).
46	44	IR ν_{max} (Nujol)/cm^{-1} 3094, 2926, 2855, 1716, 1593, 1523, 1489, 1468, 1421, 1332 and 1190; NMR δ_H (400 MHz, $CDCl_3$) 8.00 (1H, m), 7.78 (1H, m), 7.50 (2H, m), 6.62 (1H, m), 4.15 (2H, m), 3.40 (2H, m), 2.95 (2H, m) and 1.20 (3H, t, *J* 7.0 Hz); M/Z 303 $(M+H)^+$.
47		IR ν_{max} (Nujol)/cm^{-1} 3417, 3103, 2974, 2944, 2859, 2820, 2776, 1599, 1556, 1538, 1488, 1462, 1337 and 1256. NMR δ_H (400 MHz, $CDCl_3$) 7.84 (1H, d, *J* 5.5 Hz), 7.73 (1H, s), 7.38 (1H, m), 7.22 (1H, d, *J* 5.5 Hz), 6.63 (1H, m), 5.64 (1H, br s), 3.60 (2H, q, *J* 6.0 Hz), 2.59 (2H, t, *J* 6.0 Hz), 2.28 (6H, s).
48	44	NMR δ_H (400 MHz, $CDCl_3$) 8.01 (1H, m), 7.79 (1H, m), 7.50 (2H, m), 6.80 (1H, m), 4.10 (1H, br m), 3.80 (2H, m), 3.30 (2H, m) and 2.18 (2H, m); Retention time 2.42 (80:20).
49	81	IR ν_{max} (Nujol)/cm^{-1} 3079, 2923, 1745, 1729, 1698, 1594, 1531, 1466, 1336, 809; NMR δ_H (400 MHz, DMSO) 2.84 (2H, t, *J* 7.0 Hz), 3.24 (2H, t, *J* 7.0 Hz), 6.86 (1H, dd, *J* 1.8, 3.5 Hz), 7.54 (1H, dd, *J* 0.8, 3.5 Hz), 7.58 (1H, d, *J* 5.5 Hz), 8.17 (1H, dd, *J* 0.8, 1.8 Hz), 8.51 (1H, d, *J* 5.5 Hz), 12.05 (1H, br).
50	25	NMR δ_H (400 MHz, $CDCl_3$) 1.85 (2H, m), 1.95 (2H, m), 2.95 (2H, t, *J* 7.8 Hz), 3.50 (6H, m), 6.65 (1H, dd, *J* 1.7, 3.5 Hz), 7.48 (2H, m), 7.76 (1H, m), 7.99 (1H, d, *J* 5.5 Hz).
51	82	mp 145.8 – 146.5 °C; IR ν_{max} (Nujol)/cm^{-1} 3403, 3310, 3135, 1600, 1551, 1517, 1463 and 750; NMR δ_H (400 MHz, $CDCl_3$) 3.30 (6H, s), 4.13 (2H, s), 6.59 – 6.61 (2H, m), 7.35 (1H, dd, *J* 3.5, 1.0 Hz), 7.68 – 7.71 (1H, m); Anal. Calcd for $C_{12}H_{12}N_4OS + 0.3\ H_2O$: C, 54.24; H, 4.78, N, 21.08. Found: C, 54.37; H, 4.51; N, 20.93.
52	52	IR ν_{max} (Nujol)/cm^{-1} 3070, 2924, 2854, 1541, 1464, 1352, 779, 650; NMR δ_H (400 MHz, $CDCl_3$) 1.50 (3H, t, *J* 7.50 Hz), 3.20 (2H, q, *J* 7.50 Hz), 7.45 (1H, m), 7.53 (1H, d, *J* 5.6 Hz), 7.92 (1H, m), 8.07 (1H, d, *J*

		5.6 Hz), 8.79 (1H, m), 8.85 (1H, m).
53		IR ν_{max} (Nujol)/cm^{-1} 2924, 2854, 1567, 1548, 1522, 1461, 1440, 1377 and 1353; NMR δ_H (400 MHz, $CDCl_3$) 7.80 (1H, d, *J* 5.5 Hz), 7.67 (1H, d, *J* 4.0 Hz), 7.26 (1H, d, *J* 5.5 Hz), 7.02 (1H, d, *J* 4.0 Hz), 3.28 (6H, s).
54	25	NMR δ_H (400 MHz, $CDCl_3$) 3.35 (2H, m), 4.12 (2H, m), 4.41 (1H, m), 6.65 (1H, d, *J* 1.8, 3.5 Hz), 7.46 (2H, m), 7.78 (1H, d, *J* 0.8, 1.8 Hz), 8.05 (1H, d, *J* 5.5 Hz).
55	52	mp 244.4 – 244.9 °C; IR ν_{max} (Nujol)/cm^{-1} 3309, 3139, 1663, 1652, 1602, 1557, 1510, 1490, 1470, 1465, 1446, 1377 and 743; NMR δ_H (400 MHz, $CDCl_3$) 3.23 (6H, s), 6.61 – 6.63 (1H, m), 6.75 (1H, s), 7.17 – 7.22 (1H, m), 7.34 – 7.46 (5H, m), 7.72 (1H, s), 7.93 (1H, s), 8.04 (1H, s).
56	51	mp 210.9 – 211.3 °C; IR ν_{max} (Nujol)/cm^{-1} 3346, 3140, 1666, 1558, 1541, 1462 and 1377; NMR δ_H (400 MHz, $CDCl_3$) 2.29 (3H, s), 3.31 (6H, s), 6.61 – 6.64 (1H, m), 7.39 (1H, d, *J* 3.5 Hz), 7.73 (1H, d, *J* 1.0 Hz), 8.25 (1H, s), 8.30 (1H, s); Anal. Calcd for $C_{14}H_{14}N_4O_2S$: C, 55.62; H, 4.67, N, 18.52. Found: C, 55.46; H, 4.57; N, 18.27.
57	47	mp 192.2 – 192.8 °C; IR ν_{max} (Nujol)/cm^{-1} 3409, 3133, 3110, 1665, 1603, 1550, 1526, 1463, 1376 and 1261; NMR δ_H (400 MHz, $CDCl_3$) 3.33 (6H, s), 6.62 – 6.64 (1H, m), 7.40 (1H, dd, *J* 3.5, 1.0 Hz), 7.51 – 7.62 (3H, m), 7.73 – 7.74 (1H, m), 7.96 – 8.01 (2H, m), 8.45 (1H, s), 9.10 (1H, s); Anal. Calcd for $C_{19}H_{16}N_4O_2S$ + 0.75 H_2O: C, 60.38; H, 4.67, N, 14.82. Found: C, 60.47; H, 4.63; N, 14.72.
58	65	mp 183.8 – 184.3 °C; IR ν_{max} (Nujol)/cm^{-1} 3269, 3134, 3069, 1613, 1583, 1551, 1520, 1449 and 794; NMR δ_H (400 MHz, $CDCl_3$) 3.10 (3H, d, *J* 5.0 Hz), 5.09 – 5.10 (1H, s), 6.62 – 6.64 (1H, m), 7.26 (1H, d, *J* 4.5 Hz), 7.38 (1H, dd, *J* 3.5, 1.0 Hz), 7.71 – 7.73 (1H, m), 7.85 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{11}H_9N_3OS$ + 0.3 H_2O: C, 55.82; H, 4.09, N, 17.75. Found: C, 55.85; H, 3.94; N, 17.68.

59	6	mp 211.9 °C; NMR δ_H (400 MHz, $CDCl_3$) 3.09 (3H, s), 6.72 – 6.74 (1H, m), 7.40 (1H, s), 7.63 (1H, d, *J* 3.5 Hz), 7.83 (1H, d, *J* 1.0 Hz), 7.90 (1H, s); M/Z 330 $(M+H)^+$.
60	32	mp 108.3 – 108.6 °C; IR ν_{max} (Nujol)/cm^{-1} 3104, 3073, 1702, 1667, 1598, 1545, 1467, 1373, 804 and 744; NMR δ_H (400 MHz, $CDCl_3$) 2.31 (3H, s), 3.66 (3H, s), 3.96 (2H, s), 6.68 – 6.70 (1H, m), 7.42 (1H, d, *J* 5.5 Hz), 7.47 (1H, d, *J* 3.5 Hz), 7.87 (1H, d, *J* 1.0 Hz), 8.07 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{15}H_{13}N_3O_3S$ + 0.2 H_2O: C, 56.49; H, 4.23, N, 13.17. Found: C, 56.63; H, 4.14; N, 13.09; M/Z 316 $(M+H)^+$.
61	23	NMR δ_H (400 MHz, $CDCl_3$) 3.69 (2H, q, *J* 5.5 Hz), 3.90 (2H, t, *J* 4.5 Hz), 5.47 - 5.58 (1H, m), 7.03 (1H, d, *J* 4.0 Hz), 7.24 (1H, d, *J* 5.5 Hz), 7.71 (1H, d, *J* 4.0 Hz) and 7.84 (1H, d, *J* 5.5 Hz); Retention time (80/20): 5.12 min
62	82	IR ν_{max} (Nujol)/cm^{-1} 2925, 2855, 1541, 1406, 1362, 783; NMR δ_H (400 MHz, $CDCl_3$) 2.93 (3H, s), 7.45 (1H, m), 7.51 (1H, d, *J* 5.6 Hz), 7.92 (1H, m), 8.07 (1H, d, *J* 5.6 Hz), 8.76 (1H, m), 8.85 (1H, m).
63	83	IR ν_{max} (Nujol)/cm^{-1} 3048, 2926, 2855, 1541, 1468, 1335, 790; NMR δ_H (400 MHz, $CDCl_3$) 1.05 (3H, t, *J* 7.5 Hz), 2.00 (2H, sextet, *J* 7.5 Hz), 3.10 (2H, m), 7.45 (1H, m), 7.51 (1H, d, *J* 5.6 Hz), 7.92 (1H, m), 8.07 (1H, d, *J* 5.6 Hz), 8.76 (1H, m), 8.85 (1H, m).
64	26	IR ν_{max} (Nujol)/cm^{-1} 3418, 3096, 2924, 1516, 1460, 1377, 1228, 827 and 795; NMR δ_H (400 MHz, $CDCl_3$) 7.55 (1H, d, *J* 6.0 Hz), 7.69 (1H, d, *J* 3.0 Hz), 8.18 (1H, d, *J* 3.0 Hz) and 8.20 (1H, d, *J* 5.5 Hz)
65	62	mp 152 - 153 °C; IR ν_{max} (Nujol)/cm^{-1} 3056, 2925, 1566, 1532, 1464, 1354, 1132 and 792; NMR δ_H (400 MHz, $CDCl_3$) 3.32 (6H, s), 7.26 (1H, d, *J* 5.5 Hz), 7.54 (1H, d, *J*, 3.0 Hz), 7.91 (1H, d, *J* 5.5 Hz) and 8.10 (1H, d, *J* 3.0 Hz)
66	10	IR ν_{max} (Nujol)/cm^{-1} 3057, 2956, 2855, 1530, 1467, 1450; NMR δ_H (400 MHz, $CDCl_3$) 7.45 (1H, m), 7.51 (1H, d, *J* 5.6 Hz), 7.92 (1H, m), 8.07 (1H, d, *J* 5.6 Hz), 8.76 (1H, m), 8.85 (1H, m), 9.28 (1H, s).

67		IR ν_{max} (Nujol)/cm^{-1} 3288, 2956, 2925, 2554, 1597, 1584, 1557, 1523, 1459, 1427 and 1333. NMR δ_H (400 MHz, $CDCl_3$) 8.82 (1H, d, J 5.0 Hz), 8.57 (1H, d, *J* 8.0 Hz), 7.95 (1H, d, *J* 5.0 Hz), 7.92 – 7.82 (1H, m), 7.44 (7.40 (1H, m), 7.29 – 7.22 (1H, m), 5.60 (1H, br s), 4.10 (1H, br s), 3.95 – 3.92 (2H, m), 3.77 – 3.75 (2H, m).
68	87	mp 140 - 142 °C; IR ν_{max} (Nujol)/cm^{-1} 3435, 2924, 1572, 1528, 1462, 1320, 1086, 793, 702 and 600; NMR δ_H (400 MHz, $CDCl_3$) 3.73 (2H, m), 3.93 (2H, t, *J* 5.0 Hz), 5.53 - 5.66 (1H, m), 7.24 (1H, d, *J* 5.5 Hz), 7.96 (1H, d, *J* 5.5 Hz) and 8.12 (1H, d, *J* 3.0 Hz)
69	50	NMR δ_H (400 MHz, $CDCl_3$) 5.78 (1H, dd, *J* 1.8, 10.5 Hz), 6.68 (1H, dd, *J* 1.7, 3.5 Hz), 6.75 (1H, dd, *J* 1.8, 17.3 Hz), 7.05 (1H, dd, *J* 10.5, 17.3 Hz), 7.53 (1H, d, *J* 5.5 Hz), 7.55 (1H, dd, *J* 3.5, 5.5 Hz), 7.78 (1H, dd, *J* 0.8, 1.7 Hz), 8.01 (1H, d, *J* 5.5 Hz).
70	16	IR ν_{max} (Nujol)/cm^{-1} 3072, 2923, 1696, 1540, 1464, 788; NMR δ_H (400 MHz, $CDCl_3$) 1.50 (6H, d, *J* 6.9 Hz), 3.44 (1H, heptet, *J* 6.9 Hz), 7.44 (1H, ddd, *J* 1.3, 4.9, 7.5 Hz), 7.54 (1H, d, *J* 5.5 Hz), 7.93 (1H, dt, *J* 1.3, 7.5 Hz), 8.06 (1H, d, *J* 5.5 Hz), 8.81 (1H, m), 8.85 (1H, m).
71	13	mp 65.0 – 65.4 °C; IR ν_{max} (Nujol)/cm^{-1} 3326, 3090, 1598, 1558, 1488, 1466, 1330 and 1088; NMR δ_H (400 MHz, $CDCl_3$) 3.41 (3H, s), 3.63 (2H, t, *J* 5.5 Hz), 3.79 (2H, q, *J* 5.5 Hz), 5.61 (1H, t, *J* 5.0 Hz), 6.63 – 6.65 (1H, m), 7.38 (1H, d, *J* 3.0 Hz), 7.72 – 7.73 (1H, m), 7.84 (1H, s); Anal. Calcd for $C_{13}H_{12}N_3BrO_2S$: C, 44.08; H, 3.41, N, 11.86. Found: C, 43.89; H, 3.48; N, 11.77.
72	42	mp 75.4 – 76.3 °C; IR ν_{max} (Nujol)/cm^{-1} 3288, 3098, 1597, 1548, 1516, 1462, 1376, 1341 and 767; NMR δ_H (400 MHz, $CDCl_3$) 1.68 – 1.80 (1H, m), 1.83 – 2.08 (2H, m), 2.17 – 2.28 (1H, m), 3.65 – 3.81 (2H, m), 3.82 – 3.90 (1H, m), 3.97 – 4.07 (1H, m), 4.34 – 4.43 (1H, m), 6.63 – 6.65 (1H, m), 7.42 (1H, d, *J* 1.0 Hz), 7.73 – 7.74 (1H, m), 7.85 (1H, s).
73	68	IR ν_{max} (Nujol)/cm^{-1} 3061, 2925, 2854, 1727, 1595, 1523, 1484, 1467, 1377 and 1230; NMR δ_H (400 MHz, $CDCl_3$) 8.15 (1H, m), 7.82 (1H, m), 7.74 (1H, m), 7.70 (1H, m), 6.70 (1H, m), 4.60 (2H, q, J 7.0 Hz), and 1.50 (3H, t, J 7.0 Hz).

74	47	NMR δ_H (400 MHz, $CDCl_3$) 1.43 (9H, s), 3.42 (2H, q, *J* 5.5 Hz), 3.65 (2H, q, *J* 5.5 Hz), 5.34 (1H, t, *J* 5.5 Hz), 6.63 (1H, dd, *J* 2.0, 3.5 Hz), 7.20 (1H, d, *J* 5.5 Hz), 7.39 (1H, d, *J* 3.5 Hz), 7.72 (1H, dd, *J* 1.0, 1.5 Hz) and 7.85 (1H, d, *J* 5.5 Hz); Retention time 3.26 min (8:2)
75	67	NMR δ_H (400 MHz, $CDCl_3$) 1.40 (2H, br s), 2.99 (2H, t, *J* 6.0 Hz), 3.60 (2H, q, *J* 6.0 Hz), 5.40 (1H, t, *J* 5.5 Hz), 6.63 (1H, dd, *J* 2.0, 3.5 Hz), 7.22 (1H, d, *J* 5.5 Hz), 7.37 (1H, d, *J* 3.5 Hz), 7.72 (1H, dd, *J* 1.0, 2.0 Hz) and 7.84 (1H, d, *J* 5.5 Hz); Retention time 2.65 min (7:3)
76	49	mp 112 - 113 °C; IR ν_{max} (Nujol)/cm^{-1} 3089, 2925, 1561, 1352, 1136 and 794; NMR δ_H (400 MHz, $CDCl_3$) 2.60 (3H, s), 3.31 (6H, s), 7.09 (1H, s), 7.24 (1H, d, *J* 5.5 Hz) and 7.90 (1H, d, *J* 5.5 Hz)
77	5	NMR δ_H (400 MHz, $CDCl_3$) 3.61 (2H, q, *J* 6.0 Hz), 3.75 (2H, q, *J* 6.0 Hz), 5.56 (1H, t, *J* 6.0 Hz), 6.65 (1H, dd, *J* 1.5, 3.5 Hz), 7.21 (1H, d, *J* 5.5 Hz), 7.39 (1H, d, *J* 3.5 Hz) 7.75 (1H, dd, *J* 1.0, 2.0 Hz), 7.92 (1H, d, *J* 5.5 Hz) and 9.31 (1H, br s); Retention time 2.89 min (80:20)
78	51	mp 155 – 156 °C; NMR δ_H (400 MHz, $CDCl_3$) 3.86 (3H, s), 3.87 (3H, s), 4.68 (2H, d, *J* 5.5 Hz), 5.40 (1H, t, *J* 5.5 Hz), 6.62 – 6.64 (1H, m), 6.82 (1H, d, *J* 8.0 Hz), 6.94 – 6.99 (2H, m), 7.24 (1H, d, *J* 5.5 Hz), 7.37 (1H, dd, *J* 3.5, 1.0 Hz), 7.72 – 7.73 (1H, m), 7.86 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{19}H_{17}N_3O_3S$: C, 62.11; H, 4.66, N, 11.43. Found: C, 62.19; H, 4.67; N, 11.44.
79	92	mp 169.6 – 169.9 °C; NMR δ_H (400 MHz, $CDCl_3$) 5.02 (2H, s), 6.63 – 6.66 (1H, m), 7.22 (1H, d, *J* 5.5 Hz), 7.39 (1H, dd, *J* 3.5, 1.0 Hz), 7.22 – 7.74 (1H, m), 7.89 (1H, d, *J* 5.5 Hz); Anal. Calcd for $C_{10}H_7N_3OS$ + 0.2 H_2O: C, 54.38; H, 3.38, N, 19.03. Found: C, 54.69; H, 3.35; N, 18.74.
80	45	IR ν_{max} (Nujol)/cm^{-1} 2925, 2855, 1545, 1464, 1356; NMR δ_H (400 MHz, $CDCl_3$) 1.45 (3H, t, *J* 7.5 Hz), 2.61 (3H, s), 3.15 (2H, q, *J* 7.5 Hz), 7.15 (1H, s), 7.50 (1H, d, *J* 5.5 Hz), 8.02 (1H, d, *J* 5.5 Hz).
81	20	NMR δ_H (400 MHz, $CDCl_3$) 8.08 (1H, m), 7.80 (1H, m), 7.55 (2H, m), 6.70 (1H, m), 4.90 (2H, s) and 3.80 (1H, br m); Retention time 3.06 (80:20).

82	37	IR ν_{max} (Nujol)/cm^{-1} 3050, 2925, 2855, 1543, 1526, 1460, 1356; NMR δ_H (400 MHz, $CDCl_3$) 1.45 (3H, t, *J* 7.5 Hz), 3.18 (2H, q, *J* 7.5 Hz), 7.54 (1H, d, *J* 7.5 Hz), 7.61 (1H, d, *J* 3.1 Hz), 8.09 (1H, d, *J* 7.5 Hz), 8.15 (1H, d, *J* 3.1 Hz).
83		IR ν_{max} (Nujol)/cm^{-1} 3287, 3089, 2924, 2854, 1633, 1603, 1548, 1516, 1486, 1462, 1377 and 1331; NMR δ_H (400 MHz, $CDCl_3$) 1.93 (3H, s), 3.54 (2H, q, *J* 5.5 Hz), 3.69 (2H, q, *J* 5.5 Hz), 5.43 (1H, t, *J* 6.0 Hz), 6.65 (1H, dd, *J* 1.5, 3.5 Hz), 6.76 (1H, br s), 7.22 (1H, d, *J* 5.5 Hz), 7.39 (1H, dd, *J* 1.0, 3.5 Hz), 7.73 (1H, dd, *J* 1.0, 1.5 Hz) and 7.89 (1H, d, *J* 5.5 Hz); Retention time 3.08 min (70:30).
84		IR ν_{max} (Nujol)/cm^{-1} 3317, 3265, 2924, 2854, 1635, 1613, 1580, 1558, 1514, 1463, 1377 and 1335; NMR δ_H (400 MHz, $CDCl_3$), 0.90 (6H, d, *J* 5.5 Hz), 2.01 (2H, m), 2.07 (1H, m), 3.56 (2H, q, *J* 5.5 Hz), 3.68 (2H, q, *J* 5.5 Hz), 5.49 (1H, t, *J* 6.0 Hz), 6.65 (1H, dd, *J* 1.5, 3.5 Hz), 7.21 (1H, d, *J* 5.5 Hz), 7.39 (1H, dd, *J* 1.0, 3.5 Hz), 7.73 (1H, dd, *J* 1.0, 1.5 Hz) and 7.89 (1H, d, *J* 5.5 Hz); Retention time 4.43 min (70:30).
85		IR ν_{max} (Nujol)/cm^{-1} 3318, 3083, 2974, 2871, 1644, 1600 1549, 1488, 1461 and 1337; NMR δ_H (400 MHz, $CDCl_3$) 3.75 (2H, q, *J* 5.5 Hz), 3.83 (2H, q, *J* 5.5 Hz), 5.68 (1H, t, *J* 5.0 Hz), 6.62 (1H, dd, J 1.5, 3.5 Hz), 7.21 (1H, d, *J* 5.5 Hz), 7.29 (2H, m), 7.38 (2H, m), 7.71 (3H, m), 7.87 (1H, m) and 7.90 (1H, d, *J* 5.5 Hz); Retention time 5.05 min (70:30).
86		IR ν_{max} (Nujol)/cm^{-1} 3267, 3108, 2925, 2854, 1641, 1611, 1548, 1517, 1485, 1464, 1422 and 1334; NMR δ_H (400 MHz, $CDCl_3$) 3.71 (2H, q, *J* 5.5 Hz), 3.81 (2H, q, *J* 5.5 Hz), 5.65 (1H, t, *J* 6.0 Hz), 6.63 (1H, dd, *J* 1.5, 3.5 Hz), 6.92 (1H, m), 7.24 (1H, d, *J* 5.5 Hz), 7.37 (3H, m), 7.56 (1H, br s), 7.72 (1H, dd, *J* 1.0, 1.5 Hz) and 7.89 (1H, d, *J* 5.5 Hz); Retention time 4.79 min. (70:30).
87		NMR δ_H (400 MHz, $CDCl_3$) 3.52 (2H, m), 3.64 (3H, s), 3.79 (2H, m), 5.53 (1H, br s), 6.73 (1H, dd, *J* 1.5, 3.5 Hz), 7.34 (1H, d, *J* 5.5 Hz), 7.65 (1H, m), 7.83 (1H, m) and 8.02 (1H, d, *J* 5.5 Hz); Retention time 3.46 min. (70:30).

88		NMR δ_H (400 MHz, $CDCl_3$) 0.87 (6H, d, *J* 6.4 Hz), 1.83 (2H, m), 3.52 (2M, q, *J* 5.5 Hz), 3.73 (2H, m), 3.85 (2H, m), 5.50 (1H, br s) 6.71 (1H, dd, *J* 1.5, 3.5 Hz), 7.32 (1H, d, *J* 5.5 Hz), 7.61 (1H, m), 7.81 (1H, m) and 7.96 (1H, d, *J* 5.5 Hz); Retention time 5.69 min. (70:30).
89	99	NMR δ_H (400 MHz, $CDCl_3$) 3.55 (2H, q, *J* 5.8 Hz), 3.78 (2H, q, *J* 5.8 Hz), 5.07 (2H, s), 5.55 (1H, m), 6.73 (1H, dd, *J* 1.5, 3.5 Hz), 7.29 (5H, m), 7.40 (1H, d, *J* 5.5 Hz), 7.76 (1H, m), 7.85 (1H, m), 8.11 (1H, d, *J* 5.5 Hz) and 10.05 (1H, br s); Retention time 6.16 min (70:30)
90		NMR δ_H (400 MHz, $CDCl_3$) 3.01 (1H, t, *J* 5.8 Hz), 3.60 (2H, q, *J* 5.5 Hz), 4.04 (2H, d, *J* 5.8 Hz), 4.11 (2H, q, *J* 5.5 Hz), 5.46 (1H, m), 6.61 (1H, dd, *J* 1.5, 3.5 Hz), 7.31 (1H, d, *J* 5.5 Hz), 7.33 – 7.45 (4H, m), 7.71 – 7.79 (4H, m) and 7.82 (1H, d, *J* 5.5 Hz); Retention time 17.2 min (70:30).
91		NMR δ_H (400 MHz, DMSO) 3.27 (2H, m), 3.42 (2H, m), 3.63 (2H, m), 5.01 (1H, m), 5.08 (1H, m), 5.77 (1H, m), 6.10 (1H, br s), 6.85 (1H, dd, J 1.5, 3.5 Hz), 7.29 (1H, d, J 5.5 Hz), 7.48 (2H, m), 8.17 (1H, m) and 8.35 (1H, d, J 5.5 Hz); Retention time 3.39 min. (70:30).
92	99	NMR δ_H (400 MHz, DMSO) 3.30 (2H, t, *J* 6.0 Hz), 3.45 (2H, t, *J* 6.0 Hz), 4.23 (2H, s), 6.46 (1H, br s), 6.85 (1H, dd, *J* 2.0, 3.5 Hz), 7.18 – 7.33 (7H, m), 7.49 (2H, m), 8.17 (1H, m) and 8.36 (1H, d, *J* 5.5 Hz); Retention time 4.61 min (7:3)
93		NMR δ_H (400 MHz, DMSO) 1.02 – 1.25 (5H, m), 1.51 – 1.78 (5H, m), 3.26 (2H, m), 3.34 (1H, m), 3.43 (2H, m), 5.75 (1H, br s), 6.78 (1H, br s), 6.87 (1H, dd, *J* 1.5, 3.5 Hz), 7.34 (1H, d, *J* 5.5 Hz), 7.49 (1H, m), 7.96 (1H, br s), 8.15 (1H, m) and 8.36 (1H, d, *J* 5.5 Hz); Retention time 5.30 min, (70:30).
94		NMR δ_H (400 MHz, DMSO) 3.35 (2H, m), 3.44 (2H, m), 6.30 (1H, t, *J* 6.0 Hz), 6.79 (1H, dd, *J* 1.5, 3.5 Hz), 7.17 – 7.31 (5H, m), 7.36 – 7.47 (3H, m), 8.10 (1H, m), 5.27 (1H, d, *J* 5.5 Hz) and 8.52 (1H, m); Retention time 5.46 min, (70:30).

95		NMR δ_H (400 MHz, DMSO) 3.35 (2H, q, *J* 5.8 Hz), 3.46 (2H, q, *J* 5.8 Hz), 6.35 (1H, t, *J* 6.0 Hz), 6.80 (1H, dd, *J* 1.5, 3.5 Hz), 7.19 (1H, m), 7.25 (3H, m), 7.41 (3H, m), 8.10 (1H, dd, *J* 1.0, 1.5 Hz), 8.28 (1H, d, *J* 5.5 Hz) and 8.70 (1H, m); Retention time 9.61 min. (70:30).
96		NMR δ_H (400 MHz, $CDCl_3$) 3.56 (2H, q, *J* 5.8 Hz), 3.78 (2H, m), 5.07 (2H, s), 5.55 (1H, br s), 6.73 (1H, dd, *J* 1.5, 3.5 Hz), 7.29 – 7.36 (5H, m), 7.39 (1H, d, *J* 5.5 Hz), 7.76 (1H, m), 7.85 (1H, m) 8.11 (1H, d, *J* 5.5 Hz) and 10.07 (1H, br s); Retention time 6.16 min (70:30).
97		NMR δ_H (400 MHz, DMSO) 3.58 (2H, m), 3.76 (2H, m), 6.80 (1H, dd, *J* 1.5, 3.5 Hz), 7.22 (1H, d, *J* 5.5 Hz), 7.35 (4H, m), 7.42 (3H, m), 7.96 (1H, m) 8.11 (1H, m), 8.27 (1H, d, *J* 5.5 Hz) and 9.68 (1H, br s); Retention time 8.41 min, (70:30).
98		NMR δ_H (400 MHz, DMSO) 2.93 (3H, s), 3.21 (2H, m), 3.64 (2H, m), 6.86 (1H, dd, *J* 1.5, 3.5 Hz), 7.18 (1H, m), 7.32 (1H, m), 7.52 (1H, m), 7.86 (1H, m), 8.17 (1H, m) and 8.37 (1H, m); Retention time 2.93 min (70:30).
99		NMR δ_H (400 MHz, $CDCl_3$) 1.21 (9H, s), 3.28 (2H, q, J 5.8 Hz), 3.61 (2H, q, J 5.9 Hz), 5.41 (1H, t, J 6.0 Hz), 6.58 (1H, t, J 6.0 Hz) 6.65 (1H, dd, J 1.5, 3.5 Hz), 7.23 (1H, d, J 5.5 Hz), 7.40 (3H, m), 7.69 (2H, d, J 6.4 Hz), 7.74 (1H, m) and 7.87 (1H, d, J 5.5 Hz); Retention time 10.30 min
100	35	NMR δ_H (400 MHz, $CDCl_3$) 8.88 (1H, m), 8.70 (1H, m), 8.08 (1H, m), 7.88 (1H, m), 7.82 (1H, m), 7.78 (1H, m), 7.64 (2H, m) and 6.30 (1H, m); Retention time 3.52 (80:20).
101	80	mp 193.9 – 195.0 °C; IR ν_{max} (Nujol)/cm^{-1} 3246, 3149, 3080, 3064, 1683, 1664, 1599, 1547, 1497, 1315 and 1298; NMR δ_H (400 MHz, DMSO) 2.26 (3H, s), 6.86 – 6.88 (1H, m), 7.51 (1H, d, *J* 3.0 Hz), 7.48 (1H, d, *J* 5.5 Hz), 8.20 (1H, s), 8.51 (1H, d, *J* 5.5 Hz), 10.58 (1H, s); Anal. Calcd for $C_{12}H_9N_3O_2S$ + 0.5 H_2O: C, 53.72; H, 3.76, N, 15.66. Found: C, 53.81; H, 3.44; N, 15.41.
102		Mp 243 – 244 °C, IR ν_{max} (Nujol)/cm^{-1} 2955, 2924, 2854, 1543, 1526, 1574, 1468, 1435, 1358 and 1236. NMR δ_H (400 MHz, $CDCl_3$) 8.18 (1H, d, *J* 5.5 Hz), 7.82 (1H, s), 7.53 (1H, d, *J* 5.5 Hz), 2.63 (3H, s).

103		Mp 240 – 241 °C, IR ν_{max} (Nujol)/cm^{-1} 2955, 2925, 2854, 1537, 1516, 1481, 1460, 1359 and 1230. NMR δ_H (400 MHz, $CDCl_3$) 8.15 (1H, d, *J* 5.5 Hz), 7.51 (1H, d, *J* 5.5 Hz), 2.50 (6H, s).
104	71	mp 208 - 211 °C; IR ν_{max} (Nujol)/cm^{-1} 2855, 1567, 1520, 1358, 1101, 817 and 794; NMR δ_H (400 MHz, $CDCl_3$) 2.57 (3H, d, *J* 1.0 Hz), 3.30 (6H, s), 7.24 (1H, d, *J* 5.5 Hz), 7.74 (1H, d, *J* 1.5 Hz) and 7.89 (1H, d, *J* 5.5 Hz)
105	99	Mp 148 - 149 °C; IR ν_{max} (Nujol)/cm^{-1} 2854, 1564, 1356, 1236 and 7932; NMR δ_H (400 MHz, $CDCl_3$) 2.45 (3H, s), 2.47 (3H, s), 3.30 (6H, s), 7.23 (1H, d, *J* 5.5 Hz) and 7.87 (1H, d, *J* 5.5 Hz)
106		Mp 170 – 170.5 °C; IR ν_{max} (Nujol)/cm^{-1} 3061, 2955, 2925, 2854, 1545, 1519, 1480, 1465,and 1377. NMR δ_H (400 MHz, $CDCl_3$) 8.09 (1H, d, *J* 5.5 Hz), 7.88 (2H, d, *J* 7.0 Hz), 7.71 (1H, s), 7.57 (1H, d, *J* 5.5 Hz), 7.50 (2H, t, *J* 7.5 Hz), 7.42 (1H, t, *J* 7.5 Hz), 3.25 (2H, q, *J* 7,5 Hz), 1.53 (3H, t, *J* 7.5 Hz).
107		Mp 258 – 258.5 °C; IR ν_{max} (Nujol)/cm^{-1} 3136, 3073, 2955, 2924, 2854, 1573, 1559, 1514, 1475, 1408, 1335 and 1251. NMR δ_H (400 MHz, $CDCl_3$) 10.43 (1H, br s), 7.91 (1H, d, *J* 5.5 Hz), 7.43 (1H, s), 7.25 – 7.21 (2H, m), 3.30 (6H, s)
108	80	Mp 178.7 – 179.5 °C; IR ν_{max} (Nujol)/cm^{-1} 3245, 2924, 2845, 1600, 1554, 1530, 1515, 1467, 1344, 1321, 1251 and 1232, NMR δ_H (400 MHz, $CDCl_3$) 8.11 (1H, d, *J* 3.2 Hz), 7.97 (1H, m), 7.55 (1H, d, *J* 3.2 Hz), 7.25 (1H, s), 7.00 (1H, s), 6.98 (1H, m), 6.84 (1H, m), 5.46 (1H, t, *J* 5.6 Hz), 4.70 (2H, d, *J* 6.0 Hz), 3.87 (3H, s) and 3.87 (3H, s); Anal Calcd. for $C_{18}H_{16}N_4O_2S_2$: C, 56.23; H, 4.19; N, 14.57. Found: C, 56.23; H, 4.11; N 14.41.
109		Mp 221 - 222 °C; IR ν_{max} (Nujol)/cm^{-1} 3083, 2925, 2854, 1528, 1519, 1461, 1377, 1303, 1241 and 1161. NMR δ_H (400 MHz, $CDCl_3$) 8.68 (1H, s), 8.63 (1H, d, *J* 8.0 Hz), 8.17 (1H, d, *J* 5.5 Hz), 7.74 (1H, d, *J* 8.0 Hz), 7.52 (1H, d, *J* 5.5 Hz), 2.48 (3H, s).

110	63	mp 190.1 – 190.7 °C; IR ν_{max} (Nujol)/cm^{-1} 3464, 3296, 3165, 3122, 3038, 1635, 1555, 1541, 1481 and 1360; NMR δ_H (400 MHz, $CDCl_3$) 5.10 (2H, s), 7.24 (1H, d, *J* 5.5 Hz), 7.58 (1H, d, *J* 3.0 Hz), 7.98 (1H, d, *J* 5.5 Hz), 8.12 (1H, d, *J* 3.0 Hz); Anal. Calcd for $C_9H_6N_4S_2$: C, 46.14; H, 2.58, N, 23.90. Found: C, 46.14; H, 2.67; N, 23.02.
111	85	mp 139.3 – 139.7 °C; IR ν_{max} (Nujol)/cm^{-1} 3326, 3118, 3078, 3062, 1557, 1537, 1506, 1356 and 795; NMR δ_H (400 MHz, $CDCl_3$) 1.75 – 7.84 (1H, m), 1.91 – 2.10 (2H, m), 2.15 – 2.26 (1H, m), 3.70 – 3.82 (2H, m), 3.84 – 3.98 (2H, m), 4.38 – 4.56 (1H, s), 7.24 (1H, d, *J* 5.5 Hz), 7.56 (1H, d, *J* 3.5 Hz), 7.95 (1H, d, *J* 5.5 Hz), 8.12 (1H, d, *J* 3.5 Hz); Anal. Calcd for $C_{14}H_{14}N_4OS_2$: C, 52.81; H, 4.43, N, 17.59. Found: C, 53.08; H, 4.53; N, 17.22.
112	62	mp 128 – 129 °C; IR ν_{max} (Nujol)/cm^{-1} 3251, 3102, 3076, 3019, 1596, 1552, 1528, 1448, 1336 and 794; NMR δ_H (400 MHz, $CDCl_3$) 4.19 – 4.24 (2H, m), 5.14 – 5.37 (3H, m), 5.99 – 6.10 (1H, m), 7.24 (1H, d, *J* 5.5 Hz), 7.56 (1H, d, *J* 3.0 Hz), 7.95 (1H, d, *J* 5.5 Hz), 8.11 (1H, d, *J* 3.0 Hz).
113	84	mp 90.6 - 90.7 °C; IR ν_{max} (Nujol)/cm^{-1} 3056, 2961, 2855, 1546, 1529, 1480, 806; NMR δ_H (400 MHz, $CDCl_3$) 1.48 (6H, d, *J* 6.9 Hz), 3.40 (1H, heptet, *J* 6.9 Hz), 7.55 (1H, d, *J* 5.5 Hz), 7.59 (1H, d, *J* 3.1 Hz), 8.08 (1H, d, *J* 5.5 Hz), 8.14 (1H, d, *J* 3.1 Hz).
114	7	IR ν_{max} (Nujol)/cm^{-1} 2925, 2854, 1615, 1545, 1498, 1459, 1377, 1265 and 1174; NMR δ_H (400 MHz, $CDCl_3$) 8.05 (1H, m), 7.80 (1H, m), 7.60 (2H, m), 7.00 (1H, m), 3.83 (3H, s), 3.25 (2H, q, J 7.0 Hz) and 1.50 (3H, t, J 7.0 Hz).
115	93	mp 133 - 133.5 °C; IR ν_{max} (Nujol)/cm^{-1} 2925, 1553, 1467, 1404, 1356, 1241 and 796; NMR δ_H (400 MHz, $CDCl_3$) 2.44 (3H, s), 3.35 (6H, s), 7.25 (1H, d, *J* 5.5 Hz), 7.67 (1H, dd, *J* 7.5, 2.5 Hz), 7.89 (1H, d, *J* 5.5 Hz), 8.54 (1H, d, *J* 8.5 Hz) and 8.64 (1H, d, *J* 2.0 Hz)
116	37	mp 242.6 – 243.9 °C; IR ν_{max} (Nujol)/cm^{-1} 3251, 3079, 3060, 1687, 1672, 1560, 1496 and 1320; NMR δ_H (400 MHz, DMSO) 2.29 (3H, s), 7.54 (1H, d, *J* 5.5 Hz), 8.15 (1H, d, *J* 3.5 Hz), 8.27 (1H, d, *J* 3.0 Hz), 8.56 (1H, d, *J* 5.5 Hz), 10.68 (1H, s).

117	67	Mp 149 °C; IR ν_{max} (Nujol)/cm^{-1} 2955, 2925, 2854, 1595, 1523, 1485, 1468 and 1333; NMR δ_H (400 MHz, $CDCl_3$) 8.00 (1H, m), 7.76 (1H, m), 7.60 (1H, m), 7.56 (1H, m), 7.36 (1H, m), 7.05 (1H, m), 6.92 (1H, m), 6.63 (1H, m) and 4.59 (2H, s).
118		IR ν_{max} (Nujol)/cm^{-1} 3036, 2925, 2854, 1535, 1481, 1468, 1351, 1129 and 1098; NMR δ_H (400 MHz, $CDCl_3$) 9.01 (1H, m), 8.78 (1H, s), 8.01 (1H, d, J 5.6 Hz), 7.57 (1H, d, J 5.2 Hz), 3.13 (2H, q, J 7.6 Hz) and 1.47 (3H, t, J 7.6 Hz).
119	3	Mp 179 °C; IR ν_{max} (Nujol)/cm^{-1} 3057, 2924, 2854, 1525, 1465, 1438, 1378 and 1296; NMR δ_H (400 MHz, $CDCl_3$) 8.12 (2H, m), 7.58 (2H, m), 3.30 (4H, q, J 7.0 Hz) and 1.60 (6H, t, J 7.0 Hz); M/Z 327 $(M+H)^+$.
120		IR ν_{max} (Nujol)/cm^{-1} 3388, 3060, 2924, 2855, 1662, 1561, 1541, 1461, 1376, 1356, 1309, 1266 and 1096. NMR δ_H (400 MHz, $CDCl_3$) 8.32 (1H, br s), 8.13 (1H, d, *J* 5.5 Hz), 7.58 (1H, *J* 5.5 Hz), 7.26 (1H, s), 3.19 (2H, q, *J* 7.5 Hz), 1.48 (3H, t, *J* 7.5 Hz).
121	39	mp 178.6 - 179.6 °C; IR ν_{max} (Nujol)/cm^{-1} 3080, 2925, 1569, 1525, 1468, 1092, 854, 815 and 750; NMR δ_H (400 MHz, $CDCl_3$) 1.47 (3H, t, *J* 7.5 Hz), 3.11 (2H, q, *J* 7.5 Hz), 7.29 (1H, s), 7.47 (1H, s), 7.51 (1H, d, *J*, 5.5 Hz), 8.07 (1H, d, *J* 5.5 Hz) and 10.65 (1H, br s)
122	13	Mp 131 °C; IR ν_{max} (Nujol)/cm^{-1} 2960, 1547, 1529, 1377, 1314, 1301 and 1096; NMR δ_H (400 MHz, $CDCl_3$) 8.24 (1H, m), 8.12 (1H, m), 8.02 (1H, m), 7.48 – 7.60 (3H, m), 3.20 (2H, q, J 7.0 Hz) and 1.50 (3H, t, J 7.0 Hz).
123	73	IR ν_{max} (Nujol)/cm^{-1} 3392, 3254, 1681, 1586, 1552, 1515, 1342, 1318, 1274, 1252, 1165 and 1150; NMR δ_H (400 MHz, $CDCl_3$) 1.43 (9H, s), 3.46 (2H, q, *J* 5.5 Hz), 3.70 (2H, q, *J* 5.5 Hz), 5.12 (1H, br s), 5.42 (1H, t, *J* 5.5 Hz), 7.23 (1H, d, *J* 5.5 Hz), 7.55 (1H, d, *J* 3.5 Hz), 7.95 (1H, d, *J* 5.5 Hz) and 8.11 (1H, d, *J* 3.0 Hz); Retention time 5.17 min (70:30)
124	60	IR ν_{max} (Nujol)/cm^{-1} 3352, 3241, 3045, 1558, 1349, 1315, 1280 and 1116; NMR δ_H (400 MHz, $CDCl_3$) 1.27 (2H, br s), 3.02 (2H, t, *J* 6.0 Hz), 3.63 (2H, q, *J* 6.0 Hz), 5.46 (1H, m), 7.23 (1H, d, *J* 5.5 Hz), 7.55 (1H, d, *J* 3.5 Hz), 7.94 (1H, d, *J* 5.5 Hz) and 8.11 (1H, d, *J* 3.5 Hz); Retention

		time 2.35 min (60:40)
125	61	NMR δ_H (400 MHz, DMSO) 1.81 (3H, s), 3.30 (2H, q, *J* 6.0 Hz), 3.44 (2H, q, *J* 6.0 Hz), 7.28 (2H, m), 7.97 (1H, m), 8.07 (1H, d, *J* 3.0 Hz), 8.21 (1H, d, *J* 3.0 Hz) and 8.32 (1H, d, *J* 5.5 Hz); Retention time 2.83 min (70:30)
126		NMR δ_H (400 MHz, DMSO) 0.97 (3H, t, *J* 7.2 Hz), 3.00 (2H, m), 3.26 (2H, q, *J* 6.0 Hz), 3.40 (2H, q, *J* 6.0 Hz), 5.86 (1H, t, *J* 5.5 Hz), 5.96 (1H, t, *J* 5.5 Hz), 7.29 (2H, m), 8.08 (1H, d, *J* 3.2 Hz), 8.22 (1H, d, *J* 3.3 Hz) and 8.32 (1H, d, *J* 5.5 Hz); Retention time 2.42 (80:20).
127		NMR δ_H (400 MHz, DMSO) 3.30 (2H, q, *J* 5.8 Hz), 3.42 (2H, q, *J* 5.8 Hz), 3.63 (2H, m), 5.00 (1H, dd, *J* 1.6, 10.2 Hz), 5.09 (1H, dd, *J* 1.8, 17.2 Hz), 5.79 (1H, m), 6.05 (2H, m), 7.29 (2H, m) 8.08 (1H, d, J 3.1 Hz), 8.22 (1H, d, *J* 3.1 Hz) and 8.32 (1H, d, *J* 5.5 Hz); Retention time 2.50 min (80:20).
128	81	NMR δ_H (400 MHz, DMSO) 0.99 – 1.28 (5H, m), 1.48 – 1.74 (5H, m), 3.25 (2H, q, *J* 6.0 Hz), 3.33 (1H, m), 3.39 (2H, q, *J* 6.0 Hz), 5.77 (1H, d, *J* 8.0 Hz), 5.86 (1H, t, *J* 5.5 Hz), 7.28 (1H, m), 8.07 (1H, d, *J* 3.0 Hz), 8.21 (1H, d, *J* 3.0 Hz) and 8.31 (1H, d, *J* 5.5 Hz); Retention time 3.11 min (80:20)
129	42	NMR δ_H (400 MHz, DMSO) 0.84 (6H, d, *J* 6.5 Hz), 1.95 (3H, m), 3.37 (2H, m), 3.43 (2H, q, *J* 6.0 Hz), 7.26 (2H, m), 7.89 (1H, m), 8.08 (1H, d, *J* 3.0 Hz), 8.21 (1H, d, *J* 3.0 Hz) and 8.32 (1H, d, *J* 5.5 Hz); Retention time 2.77 min (80:20)
130	58	NMR δ_H (400 MHz, DMSO) 3.25 (2H, q, *J* 6.0 Hz), 3.44 (2H, q, *J* 6.0 Hz), 3.52 (3H, s), 7.21 (1H, t, *J* 5.5 Hz), 7.26 (1H, d, *J* 5.5 Hz), 7.30 (1H, m), 8.07 (1H, d, *J* 3.0 Hz), 8.21 (1H, d, *J* 3.0 Hz) and 8.32 (1H, d, *J* 5.5 Hz); Retention time 2.53 min (80:20)
131	62	NMR δ_H (400 MHz, DMSO) 0.84 (6H, d, *J* 6.5 Hz), 1.79 (1H, m), 3.25 (2H, q, *J* 6.0 Hz), 3.45 (2H, q, *J* 6.0 Hz), 3.71 (2H, d, *J* 6.5 Hz), 7.16 (1H, t, *J* 5.5 Hz), 7.26 (1H, d, *J* 5.5 Hz), 7.30 (1H, m), 8.07 (1H, d, *J* 3.0

		Hz), 8.21 (1H, d, *J* 3.0 Hz) and 8.32 (1H, d, *J* 5.5 Hz); Retention time 3.23 min (80:20)
132		NMR δ_H (400 MHz, DMSO) 1.21 (9H, s), 3.24 (2H, q, *J* 5.8 Hz), 3.39 (2H, q, *J* 5.8 Hz), 5.68 (1H, s), 5.80 (1H, t, *J* 6.0 Hz), 7.28 (2H, m), 8.07 (1H, d, *J* 3.1 Hz), 8.22 (1H, d, *J* 3.1 Hz), and 8.32 (1H, d, *J* 5.5 Hz); Retention time 2.83 min, (80:20).
133	95	NMR δ_H (400 MHz, DMSO) 3.30 (2H, q, *J* 6.0 Hz), 3.42 (2H, q, *J* 6.0 Hz), 4.20 (2H, d, *J* 5.6 Hz), 6.10 (1H, t, *J* 5.9 Hz), 6.41 (1H, t, *J* 6.0 Hz), 7.16 – 7.33 (7H, m), 8.07 (1H, d, *J* 3.5 Hz), 8.21 (1H, d, *J* 3.0 Hz) and 8.31 (1H, d, *J* 5.5 Hz); Retention time 2.87 min (80:20)
134		NMR δ_H (400 MHz, DMSO) 3.38 (2H, q, *J* 5.8 Hz), 3.47 (2H, q, *J* 5.8 Hz), 6.29 (1H, t, *J* 6.0 Hz), 6.88 (1H, t, *J* 6.0 Hz), 7.21 (1H, t, *J* 6.0 Hz), 7.27 (3H, m), 7.37 (3H, m), 8.07 (1H, d, *J* 3.1 Hz), 8.22 (1H, d, *J* 3.2 Hz) and 8.32 (1H, d, *J* 5.5 Hz); Retention time 3.22 min (80:20).
135		NMR δ_H (400 MHz, DMSO) 3.38 (2H, q, *J* 5.8 Hz), 3.48(2H, q, *J* 5.8 Hz), 6.33 (1H, t, *J* 6.0 Hz), 7.27 (3H, m), 7.40 (3H, m), 8.06 (1H, d, *J* 3.1 Hz), 8.21 (1H, d, *J* 3.1 Hz), 8.32 (1H, d, *J* 5.5 Hz) and 8.67 (1H, s); Retention time 4.32 min (80:20).
136		NMR δ_H (400 MHz, DMSO) 1.08 – 1.32 (6H, m), 1.51 – 1.85 (4H, m), 3.53 (2H, m), 3.62 (3H, m), 7.29 (2H, m), 7.36 (1H, m), 8.08 (1H, d, *J* 3.1 Hz), 8.22 (1H, d, *J* 3.1 Hz) and 8.31 (1H, d, *J* 5.5 Hz); Retention time 3.58 min. (80:20).
137		NMR δ_H (400 MHz, DMSO) 3.60 (2H, m), 3.79 (2H, m), 7.07 (1H, t, *J* 6.0 Hz), 7.26 (3H, m), 7.36 (2H, m), 7.42 (1H, m), 7.83 (1H, br s), 8.07 (1H, d, *J* 3.2 Hz), 8.22 (1H, d, *J* 3.2 Hz), 8.32 (1H, d, *J* 5.5 Hz) and 9.58 (1H, br s); Retention time 2.98 min (80:20).
138	99	NMR δ_H (400 MHz, DMSO) 3.59 (2H, q, *J* 6.0 Hz), 3.78 (2H, m), 7.25 (1H, d, *J* 5.5 Hz), 7.29 (2H, d, *J* 9.1 Hz), 7.41 (1H, m), 7.42 (2H, d, *J* 9.0 Hz), 7.95 (1H, m), 8.07 (1H, d, *J* 3.5 Hz), 8.21 (1H, d, *J* 3.0 Hz), 8.32 (1H, d, *J* 5.5 Hz) and 9.63 (1H, br s); Retention time 3.98 min (80:20)

139	93	IR ν_{max} (Nujol)/cm^{-1} 3063, 2926, 2855, 1547, 1530, 1466; NMR δ_H (400 MHz, $CDCl_3$) 1.55 (9H, s), 7.56 (1H, d, *J* 7.5 Hz), 7.58 (1H, d, *J* 3.1 Hz), 8.60 (1H, d, *J* 7.5 Hz), 8.18 (1H, d, *J* 3.1 Hz).
140	13	IR ν_{max} (Nujol)/cm^{-1} 3061, 2924, 1550, 1531, 1480; NMR δ_H (400 MHz, $CDCl_3$) 1.10 (2H, m), 1.24 (2H, m), 2.39 (1H, m), 7.42 (1H, d, *J* 7.5 Hz), 7.58 (1H, d, *J* 3.1 Hz), 8.00 (1H, d, *J* 7.5 Hz), 8.10 (1H, d, *J* 3.1 Hz).
141	65	mp 74.7 - 74.9 °C; IR ν_{max} (Nujol)/cm^{-1} 2925, 1531, 1455, 1350, 1078, and 799; NMR δ_H (400 MHz, $CDCl_3$) 1.52 (3H, t, *J* 7.5 Hz), 2.74 (3H, s), 3.19 (2H, q, *J* 7.5 Hz), 7.29 (1H, d, *J* 7.5 Hz), 7.52 (1H, d, *J* 6.0 Hz), 7.80 (1H, t, *J* 8.0 Hz), 8.06 (1H, d, *J* 5.5 Hz) and 8.58 (1H, d, *J* 8.0 Hz)
142		NMR δ_H (400 MHz, DMSO) 8.32 (1H, m), 8.22 (1H, m), 8.08 (1H, m), 7.79 (1H, m), 7.34 – 7.26 (2H, m), 3.45 – 3.29 (4H, m), 2.19 (1H, m) and 1.81 – 1.15 (10H, m); Retention time 3.26 min, (80:20).
143		NMR δ_H (400 MHz, DMSO) 8.59 (1H, br s), 8.33 (1H, m), 8.22 (1H, m), 8.08 (1H, m), 7.94 (1H, m), 7.85 (2H, m), 7.63 (1H, m), 7.52 – 7.43 (1H, m), 7.28 (1H, m) and 3.60 – 3.37 (4H, br m); Retention time 3.03 min, (80:20).
144		NMR δ_H (400 MHz, DMSO) 8.66 (1H, br s), 8.33 (1H, m), 8.22 (1H, m), 8.08 (1H, m), 7.88 (2H, m), 7.52 (2H, m), 7.45 (1H, br s), 7.27 (1H, m), 3.59 – 3.54 (2H, br m) and 3.30 – 3.20 (2H, m); Retention time 3.95 min, (80:20).
145	70	NMR δ_H (400 MHz, DMSO) 3.36 (2H, q, *J* 6.0 Hz), 3.46 (2H, q, *J* 6.0 Hz), 7.12 (1H, dd, *J* 4.0, 5.0 Hz), 7.26 (1H, d, *J* 5.5 Hz), 7.72 (1H, m), 7.88 (1H, d, *J* 5.0 Hz), 8.07 (1H, d, *J* 3.0 Hz), 8.21 (1H, d, *J* 3.5 Hz), 8.32 (1H, d, *J* 5.5 Hz) and 8.60 (1H, m); Retention time 2.98 min (80:20)
146	45	NMR δ_H (400 MHz, DMSO) 3.34 (2H, q, *J* 6.0 Hz), 3.53 (2H, q, *J* 6.0 Hz), 7.22 – 7.40 (8H, m), 8.08 (1H, d, *J* 3.0 Hz), 8.22 (1H, d, *J* 3.0 Hz) and 8.33 (1H, d, *J* 5.5 Hz); Retention time 3.08 min (80:20)
147	62	NMR δ_H (400 MHz, DMSO) 3.28 (2H, q, *J* 6.0 Hz), 3.46 (2H, q, *J* 6.0 Hz), 5.01 (2H, s), 7.22 – 7.38 (8H, m), 8.07 (1H, d, *J* 3.0 Hz), 8.21 (1H, d, *J* 3.5 Hz) and 8.32 (1H, d, *J* 5.5 Hz); Retention time 3.39 min (80:20)

148	29	NMR δ_H (400 MHz, DMSO) 2.92 (3H, s), 3.22 (2H, q, *J* 6.0 Hz), 3.51 (2H, q, *J* 6.0 Hz), 7.14 (1H, t, *J* 5.9 Hz), 7.31 (1H, d, *J* 5.5 Hz), 7.35 (1H, m), 8.08 (1H, d, *J* 3.5 Hz), 8.22 (1H, d, *J* 3.5 Hz) and 8.34 (1H, d, *J* 5.5 Hz); Retention time 2.36 min (80:20)
149	70	NMR δ_H (400 MHz, DMSO) 0.83 (3H, t, *J* 7.5 Hz), 1.32 (2H, m), 1.60 (2H, m), 2.99 (2H, m), 3.20 (2H, q, *J* 6.0 Hz), 3.49 (2H, q, *J* 6.0 Hz), 7.15 (1H, t, *J* 5.9 Hz), 7.26 (1H, d, *J* 5.6 Hz), 7.32 (1H, m), 8.08 (1H, d, *J* 3.0 Hz), 8.22 (1H, d, *J* 3.0 Hz) and 8.33 (1H, d, *J* 5.5 Hz); Retention time 2.82 min (80:20)
150	22	NMR δ_H (400 MHz, $CDCl_3$) 1.34 (3H, d, *J* 6.5 Hz), 3.71 (1H, dd, *J* 6.7, 10.7 Hz), 3.85 (1H, dd, *J* 3.0, 11.0 Hz), 4.29 (1H, m), 5.20 (1H, d, *J* 6.5 Hz), 7.22 (1H, d, *J* 5.5 Hz), 7.56 (1H, d, *J* 3.5 Hz), 7.95 (1H, d, *J* 5.5 Hz) and 8.11 (1H, d, *J* 3.0 Hz); Retention time 2.67 min (80:20)
151	33	NMR δ_H (400 MHz, $CDCl_3$) 2.21 (2H, quintet, *J* 6.7 Hz), 3.59 (2H, q, *J* 6.5 Hz), 4.12 (2H, t, *J* 7.0 Hz), 5.20 (1H, t, *J* 6.0 Hz), 6.98 (1H, m), 7.09 (1H, m), 7.24 (1H, d, *J* 5.5 Hz), 7.55 (1H, m), 7.56 (1H, d, *J* 3.0 Hz), 7.97 (1H, d, *J* 5.5 Hz) and 8.12 (1H, d, *J* 3.0 Hz); Retention time 2.65 min (80:20)
152	64	NMR δ_H (400 MHz, $CDCl_3$) 1.80 (1H, m), 1.97 (1H, m), 2.03 (1H, m), 2.20 (1H, m), 3.71 – 3.80 (2H, m), 3.85 – 3.97 (2H, m), 4.41 (1H, m), 7.23 (1H, d, *J* 5.5 Hz), 7.57 (1H, d, *J* 3.0 Hz), 7.94 (1H, d, *J* 5.5 Hz) and 8.12 (1H, d, *J* 3.0 Hz); Retention time 3.63 min (80:20)
153	23	Mp 221.9 °C; IR ν_{max} (Nujol)/cm^{-1} 3069, 2923, 2854, 1539, 1523, 1465, 1377, 1366 and 1319; NMR δ_H (400 MHz, $CDCl_3$) 8.16 (2H, m), 8.10 (1H, m), 7.64 (1H, m), 7.58 (1H, m), 7.50 (1H, m) and 7.20 (1H, m).
154	50	IR ν_{max} (Nujol)/cm^{-1} 3074, 2924, 1546, 1529, 1473 and 1350; NMR δ_H (400 MHz, $CDCl_3$) 3.60 (2H, m), 4.15 (2H, m), 7.42 (1H, d, *J* 7.5 Hz), 7.58 (1H, d, *J* 3.1 Hz), 8.1 (1H, d, *J* 7.5 Hz), 8.15 (1H, d, *J* 3.1 Hz).
155	67	mp 300 °C dec; IR ν_{max} (Nujol)/cm^{-1} 3472, 3051, 2925, 2853, 1707, 1598, 1525, 1466, 791, 742, 506; NMR δ_H (400 MHz, DMSO) 6.91 (1H, dd *J* 1.7, 3.6 Hz), 7.75 (1H, d, *J* 5.5 Hz), 7.82 (1H, br), 7.89 (1H, dd, *J* 0.8, 3.6 Hz), 8.23 (1H, dd, *J* 0.8, 1.7 Hz), 8.40 (1H, br), 8.64 (1H, d, *J* 5.5

		Hz).
156		Mp 117.7 - 118.2 °C; IR v_{max} (Nujol)/cm^{-1} 3062, 2924, 2854, 1545, 1528, 1517, 1465, 1378, 1239 and 1134; NMR δ_H (400 MHz, $CDCl_3$) 8.39 (1H, m), 8.08 (1H, d, *J* 5.5 Hz), 7.98 (1H, dd, *J* 5.1, 1.1 Hz), 7.55 (1H, d, *J* 5.5 Hz) and 7.52 (1H, dd, *J* 5.1, 2.8 Hz); Anal Calcd for $C_{10}H_5ClN_2S_2$ 0.5 H_2O: C45.89; H, 2.31; N, 10.70. Found C, 45.48; H, 2.18; N, 10.53.
157	84	Mp 119.0 – 119.4 °C; IR v_{max} (Nujol)/cm^{-1} 2924, 2854, 1557, 1524, 1468, 1388, 1334, 1279, 1234 and 1092; NMR δ_H (400 MHz, $CDCl_3$) 8.23 (1H, dd, *J* 2.9, 1.3Hz), 7.95 (1H, dd, J 5.0, 1.0 Hz), 7.45 (1H, dd, *J* 5.1, 3.0 Hz), 7.27 (1H, m) and 3.31 (6H, s). Anal Calcd for $C_{12}H_{11}N_3S_2$: C, 55.15; H, 4.24; N, 16.07. Found: C55.36; H, 4.22; N, 16.05
158	28	Mp 146.5 – 147.2 °C; IR v_{max} (Nujol)/cm^{-1} 3054, 2925, 2854, 1537, 1516, 1495, 1467, 1365, 1244 and 1138; NMR δ_H (400 MHz, $CDCl_3$) 8.20 (2H, m), 8.11 (1H, d, *J* 5.6 Hz), and 7.62 – 7.57 (4H, m); Anal Calcd for $C_{12}H_7ClN_2S$ 0.25 H_2O; C, 57.37; H, 3.01; N, 11.15. Found: C, 57.25; H, 2.84; N, 11.40.
159	97	Mp 112.9 – 114.1 °C; IR v_{max} (Nujol)/cm^{-1} 2924, 2854, 1585, 1556, 1523, 1468, 1409, 1355 and 1241, NMR δ_H (400 MHz, $CDCl_3$) 8.18 (2H, m), 7.80 (1H, d, *J* 5.5 Hz), 7.56 – 7.51(3H, m), 7.29 (1H, d, *J* 5.5 Hz) and 3.33 (6H, s). Anal. Calcd for $C_{14}H_{13}N_3S$ 0.1 H_2O: C, 65.39; H, 5.13; N, 16.45; Found: C, 65.18; H, 5.14; N, 16.16.
160	33	Mp 129.3 – 129.9 °C; IR v_{max} (Nujol)/cm^{-1} 3117, 2955, 2924, 2854, 1576, 1542, 1527, 1512, 1472, 1382, 1264, 1243, 1226, 1184 and 1155, NMR δ_H (400 MHz, $CDCl_3$) 8.40 (1H, s), 8.05 (1H, d, *J* 5.5 Hz), 7.62 (1H, m), 7.54 (1H, d, *J* 5.5 Hz), and 7.22 (1H, m); Anal. Calcd for $C_{10}H_5ClN_2OS$: C, 50.75; H, 2.13; N, 11.83. Found: C, 50.71; H, 2.13; N, 11.72.
161	50	Mp 98.4 – 99.0 °C; IR v_{max} (Nujol)/cm^{-1} 2924, 2854, 1562, 1540, 1527, 1463, 1404, 1381, 1348 and 1229, NMR δ_H (400 MHz, $CDCl_3$) 8.27 (1H, d, *J* 1.2 Hz), 7.76 (1H, d, *J* 5.4 Hz), 7.55 (1H, m), 7.26 (1H, m), 7.17

		(1H, d, *J* 1.2 Hz), and 3.28 (6H, s); Anal Calcd. for $C_{12}H_{11}N_5OS$ 0.1 H_2O: C, 58.33; H, 4.57; N, 17.01. Found: C, 58.59; H, 4.56; N, 16.69.
162	31	Mp 204.0 – 204.9 °C; IR ν_{max} (Nujol)/cm^{-1} 2926, 2854, 1590, 1526, 1494, 1465, 1377, 1335 and 1268, NMR δ_H (400 MHz, DMSO) 8.71 (1H, s), 8.33 (1H, d, *J* 1.2 Hz), 7.76 (1H, d, *J* 4.1 Hz), and 6.95 (1H, dd, *J* 3.8, 1.8 Hz); Anal Calcd for $C_{10}H_4ClN_3O_2S$ 0.1 H_2O: C,42.37; H,1.49; N, 14.82. Found: C, 42.01; H, 1.42; N, 14.75.
163	69	IR ν_{max} (Nujol)/cm^{-1} 2924, 2854, 1585, 1547, 1529, 1463, 1377 and 1154; NMR δ_H (400 MHz, $CDCl_3$) 8.39 (1H, m), 7.95 (1H, m), 7.62 (1H, m), 7.53 (1H, m), 7.24 (1H, m), 3.10 (2H, d, J 7.0 Hz) and 1.42 (3H, t, J 7.0 Hz); M/Z 231 $(M+H)^+$.
164	41	IR ν_{max} (Nujol)/cm^{-1} 2925, 2854, 1615, 1546, 1526, 1482, 1463, 1420 and 1376; NMR δ_H (400 MHz, $CDCl_3$) 8.00 (1H, m), 7.58 (1H, m), 3.18 (2H, m), 2.50 (3H, s), 2.39 (3H, s) and 1.43 (3H, m); M/Z 260 $(M+H)^+$.
165		IR ν_{max} (Nujol)/cm^{-1} 3093, 2955, 2924, 2854, 1589, 1572, 1538, 1522, 1467 and 1253. NMR δ_H (400 MHz, $CDCl_3$) 9.45 (1H, d, *J* 2.0 Hz), 8.85 (1H, m), 8.54 – 8.51 (1H, m), 8.18 (1H, d, *J* 5.5 Hz), 7.62 (1H, d, *J* 5.5 Hz), 7.56 – 7.53 (1H, m).
166		IR ν_{max} (Nujol)/cm^{-1} 3056, 2925, 2854, 1580, 1557, 1524, 1467, 1361 and 1249. NMR δ_H (400 MHz, $CDCl_3$) 9.43 (1H, d, *J* 1.8 Hz), 8.76 (1H, dd, *J* 4.7, 1.5 Hz), 8.48 – 8.45 (1H, m), 7.83 (1H, d, *J* 5.5 Hz), 7.53 – 7.46 (1H, m), 7.32 (1H, d, *J* 5.5 Hz), 3.32 (6H, s).
167		NMR δ_H (400 MHz, $CDCl_3$) 8.12 (1H, d, *J* 5.5 Hz), 7.49 (1H, d, *J* 5.5 Hz), 7.38 (1H, s), 7.16 (1H, s), 7.30 (3H, s).
168		NMR δ_H (400 MHz, $CDCl_3$) 7.86 (1H, d, *J* 5.5 Hz), 7.31 (1H, s), 7.24 (1H, d, *J* 5.5 Hz), 7.06 (1H, s), 4.28 (3H, s), 3.29 (6H, s).
169		IR ν_{max} (Nujol)/cm^{-1} 3332, 3072, 2924, 2854, 1606, 1547, 1516, 1489, 1464, 1409, 1387 and 1261; NMR δ_H (400 MHz, $CDCl_3$) 7.87 1H, d, J 5.5 Hz), 7.64 (1H, d, J 1.5 Hz), 7.23 (1H, d, J 5.5 Hz), 6.57 (1H, d, J 1.5

		Hz), 5.79 (1H, t, J 7.0 Hz), 4.83 (2H, d, J 7.0 Hz), 3.28 (6H, s).
170		IR ν_{max} (Nujol)/cm^{-1} 3443, 3218, 3122, 2954, 2925, 2854, 1560, 1532, 1513, 1484, 1457, 1389 and 1318; NMR δ_H (400 MHz, $CDCl_3$) 7.90 (1H, dd, *J* 5.5, 1.8 Hz), 7.30 (1H, s), 7.20 (1H, dd, *J* 5.5, 1.8 Hz), 7.06 (1H, s), 5.46 (1H, br s), 4.22 (3H, s), 3.91 – 3.90 (2H, m), 3.72 – 3.68 (3H, m).
171		IR ν_{max} (Nujol)/cm^{-1} 3267, 3124, 2924, 2854, 1609, 1547, 1514, 1487, 1459, 1378; NMR δ_H (400 MHz, $CDCl_3$) 7.91 (1H, d, *J* 5.5 Hz), 7.65 (1H, s), 7.21 (1H, d, *J* 5.5 Hz), 6.56 (1H, s), 6.20 (1H, br s), 5.50 (1H, br s), 4.79 (2H, s), 3.90 – 3.88 (2H, m), 3.70 – 3.66 (2H, m), 1.61 (1H, br s).
172		IR ν_{max} (Nujol)/cm^{-1} 2925, 2854, 1546, 1528, 1517, 1465, 1377 and 1222; NMR δ_H (400 MHz, $CDCl_3$) 8.12 (1H, d, *J* 5.5 Hz), 7.50 (1H, d, *J* 5.5 Hz), 7.38 (1H, s), 7.20 (1H, s), 4.80 (2H, q, *J* 7.0 Hz), 1.55 (3H, t, *J* 7.0 Hz).
173		IR ν_{max} (Nujol)/cm^{-1} 3041, 2926, 2855, 1563, 1528, 1511, 1478, 1460, 1392 and 1377; NMR δ_H (400 MHz, $CDCl_3$) 7.86 (1H, d, J 5.5 Hz), 7.32 (1H, s), 7.23 (1H, d, *J* 5.5 Hz), 7.11 (1H, s), 4.83 (1H, q, *J* 7.0 Hz), 3.28 (6H, s), 1.52 (3H, t, *J* 7.0 Hz).
174		IR ν_{max} (Nujol)/cm^{-1} 3458, 3334, 2925, 2855, 1560, 1516, 1480, 1466, 1427 and 1334; NMR δ_H (400 MHz, $CDCl_3$) 7.90 (1H, d, *J* 5.5 Hz), 7.32 (1H, s), 7.19 (1H, d, *J* 5.5 Hz), 7.11 (1H, s), 5.45 (1H, br t, *J* 5.5 Hz), 4.74 (2H, q, *J* 7.0 Hz), 3.91 – 3.89 (2H, m), 3.71 – 3.67 (2H, m), 1.52 (3H, t, *J* 7.0 Hz).
175		IR ν_{max} (Nujol)/cm^{-1} 3069, 2954, 2925, 2854, 1548, 1531, 1517, 1467, 1408, 1249 and 1225; NMR δ_H (400 MHz, $CDCl_3$) 8.19 (1H, d, *J* 5.5 Hz), 7.54 (1H, d, *J* 5.5 Hz), 7.47 – 7.41 (2H, m), 6.22 (2H, s), 3.76 (2H, t, *J* 8.5 Hz), 1.02 (2H, t, *J* 8.5 Hz).
176		Mp 131 – 132 °C; IR ν_{max} (Nujol)/cm^{-1} 2924, 2854, 1560, 1533, 1512, 1480, 1465, 1419, 1389, 1250 and 1089; NMR δ_H (400 MHz, $CDCl_3$) 7.95 (1H, d, *J* 5.5 Hz), 7.43 (1H, d, *J* 1.5 Hz), 7.38 (1H, d, *J* 1.5 Hz), 7.30 (1H, d, *J* 5.5 Hz), 6.28 (2H, s), 3.66 (2H, t, 8.0 Hz), 3.36 (6H, s), 0.97

		(3H, t, *J* 8.0 Hz).
177		Mp 209 - 210 °C; IR ν_{max} (Nujol)/cm^{-1} 2925, 2854, 1749, 1559, 1530, 1508, 1476, 1388, 1376, 1241 and 1214; NMR δ_H (400 MHz, $CDCl_3$) 7.88 (1H, d, *J* 5.5 Hz), 7.37 (1H, d, *J* 1.0 Hz), 7.21 (1H, d, *J* 5.5 Hz), 7.08 (1H, d, *J* 1.5 Hz), 5.61 (2H, s), 4.18 (2H, q, *J* 7.5 Hz), 3.24 (6H, s), 1.18 (3H, t, *J* 7.0 Hz).
178		Mp 162.2 – 164.9 °C; IR ν_{max} (Nujol)/cm^{-1} 3365, 2924, 2854, 1559, 1528, 1512, 1465, 1389, 1378, 1336,and 1236; NMR δ_H (400 MHz, $CDCl_3$) 7.89 (1H, d, *J* 5.5 Hz), 7.34 (1H, d, *J* 1.0 Hz), 7.22 (1H, d, *J* 5.5 Hz), 7.19 (1H, d, *J* 1.0 Hz), 4.94 (2H, t, *J* 5.0 Hz), 4.09 (2H, br q, *J* 5.0 Hz), 3.26 (6H, s), 2.50 (1H, br t, *J* 5.0 Hz).
179		Mp 69 - 70 °C; IR ν_{max} (Nujol)/cm^{-1} 3090, 2925, 2854, 1542, 1514, 1477, 1376, 1336, 1221 and 1109; NMR δ_H (400 MHz, $CDCl_3$) 8.04 (1H, d, *J* 5.5 Hz), 7.50 (1H, d, *J* 5.5 Hz), 7.40 (1H, d, *J* 1.0 Hz), 7.34 (1H, d, *J* 1.0 Hz), 6.29 (2H, s), 3.40 (3H, s), 3.15 (2H, q, 7.5 Hz), 1.49 (3H, t, 7.5 Hz).
180		Mp <100 °C; IR ν_{max} (Nujol)/cm^{-1} 2953, 2925, 2854, 1547, 1514, 1495, 1458, 1378, 1316, 1248 and 1095; NMR δ_H (400 MHz, $CDCl_3$) 8.17 (1H, s), 8.10 (1H, d, *J* 5.5 Hz), 7.56 (1H, d, *J* 5.5 Hz), 6.41 (2H, s), 3.73 (2H, t, *J* 8.0 Hz), 3.20 (2H, q, *J* 7.5 Hz), 1.50 (3H, t, *J* 8.0 Hz), 0,90 (2H, t, *J* 8.0 Hz), 0.09 (9H, s).
181		Mp 108 - 109 °C; IR ν_{max} (Nujol)/cm^{-1} 3076, 2954, 2923, 2854, 1571, 1537, 1519, 1443, 1400, 1249, 1129 and 1116; NMR δ_H (400 MHz, $CDCl_3$) 8.49 (1H, s), 8.38 (1H, s), 8.05 (1H, d, *J* 5.5 Hz), 7.54 (1H, d, *J* 5.5 Hz), 5.55 (2H, s), 3.66 (2H, t, *J* 8.0 Hz), 0.96 (2H, t, *J* 8.5 Hz), 0.00 (9H, s).
182		Mp 141 - 142 °C; IR ν_{max} (Nujol)/cm^{-1} 2925, 2854, 1545, 1522, 1462, 1378 and 1225; NMR δ_H (400 MHz, $CDCl_3$) 8.10 (1H, d, *J* 5.5 Hz), 7.65 (1H, d, *J* 2.0 Hz) 7.57 (1H, d, *J* 5.5 Hz), 7.11 (1H, d, *J* 2.0 Hz), 4.37 (3H, s).

183		Mp 60 - 61 °C; IR ν_{max} (Nujol)/cm^{-1} 2924, 2854, 1579, 1556, 1458, 1404, 1377, 1278, 1247 and 1100; NMR δ_H (400 MHz, $CDCl_3$) 8.36 (1H, s), 8.32 (1H, s), 7.77 (1H, d, *J* 5.5 Hz), 7.27 (1H, d, *J* 5.5 Hz), 5.53 (2H, s), 3.66 2H, t, *J* 8.5 Hz) 3.30 (6H, s), 0.96 (3H, t, *J* 8.0 Hz), 0.00 (9H, s).
184		Mp 126.5 - 127 °C; IR ν_{max} (Nujol)/cm^{-1} 3052, 2954, 2924, 2854, 1553, 1515, 1465, 1412, 1386, 1353 and 1232; NMR δ_H (400 MHz, $CDCl_3$) 7.80 (1H, d, *J* 5.5 Hz), 7.60 (1H, d, *J* 2.0 Hz), 7.27 (1H, d, *J* 5.5 Hz), 7.01 (1H, d, *J* 2.0 Hz), 4.34 (3H, s), 3.29 (6H, s).
185		Mp 210 - 211 °C; IR ν_{max} (Nujol)/cm^{-1} 3146, 3090, 3058, 2924, 2854, 1582, 1556, 1465, 1404, 1377, 1277 and 1236; NMR δ_H (400 MHz, $CDCl_3$) 10.47 (1H, br s), 8.39 (2H, s), 7.77 (1H, d, *J* 5.5 Hz), 7.33 – 7.23 (1H, d, *J* 5.5 Hz), 3.30 (6H, s).
186		Mp 175.4 – 175.9 °C; IR ν_{max} (Nujol)/cm^{-1} 2925, 2854, 1548, 1458, 1407, 1383, 1279 and 1228; NMR δ_H (400 MHz, $CDCl_3$) 8.25 (1H, s), 8.15 (1H, s), 7.75 (1H, d, *J* 5.5 Hz), 7.25 (1H, d, *J* 5.5 Hz), 4.02 (3H, s), 3.29 (6H, s).
187		Mp 110.2 – 111.4 °C; NMR δ_H (400 MHz, $CDCl_3$) 8.10 (1H, d, *J* 5.5 Hz), 7.56 (1H, d, *J* 5.5 Hz), 7.26 (1H, s), 4.58 (3H, s), 3.20 (2H, q, *J* 7.5 Hz), 1.50 (3H, t, *J* 7.5 Hz).
188		Mp 104.7 – 104.8 °C; IR ν_{max} (Nujol)/cm^{-1} 3095, 2926, 2854, 1595, 1552, 1532, 1505, 1483, 1458, 1434, 1377, 1349 and 1302;p NMR δ_H (400 MHz, $CDCl_3$) 7.45 (1H, d, *J* 3.5 Hz), 7.26 (1H, s), 7.15 (1H, d, *J* 1.5 Hz), 6.64 (1H, dd, *J* 3.5 Hz, 2.0 Hz), 3.08 (2H, q, *J* 7.5 Hz), 2.69 (3H, s), 1.45 (3H, t, *J* 7.5 Hz).

Adenosine Receptor Binding

Binding Affinities at hA_{2A} Receptors

The compounds were examined in an assay measuring *in vitro* binding to human adenosine A_{2A} receptors by determining the displacement of the adenosine A_{2A} receptor selective radioligand [^{3}H]-CGS 21680 using standard techniques. The results are summarised in Table 3.

Table 3

Example	K_i (nM)
Example 15	11
Example 40	19
Example 65	2
Example 70	4
Example 71	8
Example 76	1
Example 79	14
Example 80	1
Example 82	2
Example 89	20
Example 104	5
Example 105	6
Example 110	35
Example 111	2
Example 113	1
Example 139	3
Example 140	2
Example 141	9
Example 152	3
Example 154	6

Evaluation of potential anti-Parkinsonian activity *in vivo*

Haloperidol-induced hypolocomotion model

It has previously been demonstrated that adenosine antagonists, such as theophylline, can reverse the behavioural depressant effects of dopamine antagonists, such as haloperidol, in rodents (Mandhane S.N. *et al.*, Adenosine A_2 receptors modulate haloperidol-induced

catalepsy in rats. *Eur. J. Pharmacol.* 1997, **328**, 135 - 141). This approach is also considered a valid method for screening drugs with potential antiparkinsonian effects. Thus, the ability of novel adenosine antagonists to block haloperidol-induced deficits in locomotor activity in mice can be used to assess both *in vivo* and potential antiparkinsonian efficacy.

Method
Female TO mice (25-30g) obtained from TUCK, UK, are used for all experiments. Animals are housed in groups of 8 [cage size – 40 (width) x 40 (length) x 20 (height)cm] under 12hr light/dark cycle (lights on 08:00hr), in a temperature (20 ± 2°C) and humidity (55 ± 15%) controlled environment. Animals have free access to food and water, and are allowed at least 7 days to acclimatize after delivery before experimental use.

Drugs
Liquid injectable haloperidol (1 ml Serenance ampoules from Baker Norton, Harlow, Essex, each containing haloperidol BP 5 mg, batch # P424) are diluted to a final concentration of 0.02 mg/ml using saline. Test compounds are typically prepared as aqueous suspensions in 8% Tween. All compounds are administered intraperitoneally in a volume of 10 ml/kg.

Procedure
1.5 hours before testing, mice are administered 0.2 mg/kg haloperidol, a dose that reduces baseline locomotor activity by at least 50%. Test substances are typically administered 5-60 minutes prior to testing. The animals are then placed individually into clean, clear polycarbonate cages [20 (width) x 40 (length) x 20 (height) cm , with a flat perforated, Perspex lid]. Horizontal locomotor activity is determined by placing the cages within a frame containing a 3 x 6 array of photocells linked to a computer, which tabulates beam breaks. Mice are left undisturbed to explore for 1 hour, and the number of beams breaks made during this period serves as a record of locomotor activity which is compared with data for control animals for statistically significant differences.

6-OHDA Model

Parkinson's disease is a progressive neurodegenerative disorder characterised by symptoms of muscle rigidity, tremor, paucity of movement (hypokinesia), and postural instability. It

has been established for some time that the primary deficit in PD is a loss of dopaminergic neurones in the substantia nigra which project to the striatum, and indeed a substantial proportion of striatal dopamine is lost (ca 80-85%) before symptoms are observed. The loss of striatal dopamine results in abnormal activity of the basal ganglia, a series of nuclei which regulate smooth and well co-ordinated movement (Blandini F. *et al.*, Glutamate and Parkinson's Disease, *Mol. Neurobiol.* 1996, **12**, 73 - 94). The neurochemical deficits seen in Parkinson's disease can be reproduced by local injection of the dopaminergic neurotoxin 6-hydroxydopamine into brain regions containing either the cell bodies or axonal fibres of the nigrostriatal neurones.

By unilaterally lesioning the nigrostriatal pathway on only one-side of the brain, a behavioural asymmetry in movement inhibition is observed. Although unilaterally-lesioned animals are still mobile and capable of self maintenance, the remaining dopamine-sensitive neurones on the lesioned side become supersenstive to stimulation. This is demonstrated by the observation that following systemic administration of dopamine agonists, such as apomorphine, animals show a pronounced rotation in a direction contralateral to the side of lesioning. The ability of compounds to induce contralateral rotations in 6-OHDA lesioned rats has proven to be a sensitive model to predict drug efficacy in the treatment of Parkinson's Disease.

Animals

Male Sprague-Dawley rats, obtained from Charles River, are used for all experiments. Animals are housed in groups of 5 under 12hr light/dark cycle (lights on 08:00hr), in a temperature (20 ± 2°C) and humidity (55 ± 15%) controlled environment. Animals have free access to food and water, and are allowed at least 7 days to acclimatize after delivery before experimental use.

Drugs

Ascorbic acid, desipramine, 6-OHDA and apomorphine (Sigma-Aldrich, Poole, UK). 6-OHDA is freshly prepared as a solution in 0.2% ascorbate at a concentration of 4 mg/mL prior to surgery. Desipramine is dissolved in warm saline, and administered in a volume of 1 ml/kg. Apomorphine is dissolved in 0.02% ascorbate and administered in a volume of 2 mL/kg. Test compounds are suspended in 8%Tween and injected in a volume of 2 mL/kg.

Surgery

15 minutes prior to surgery, animals are given an intraperitoneal injection of the noradrenergic uptake inhibitor desipramine (25 mg/kg) to prevent damage to non-dopamine neurones. Animals are then placed in an anaesthetic chamber and anaesthetised using a mixture of oxygen and isoflurane. Once unconscious, the animals are transferred to a stereotaxic frame, where anaesthesia is maintained through a mask. The top of the animal's head is shaved and sterilised using an iodine solution. Once dry, a 2 cm long incision is made along the midline of the scalp and the skin retracted and clipped back to expose the skull. A small hole is then drilled through the skill above the injection site. In order to lesion the nigrostriatal pathway, the injection cannula is slowly lowered to position above the right medial forebrain bundle at -3.2 mm anterior posterior, -1.5 mm medial lateral from bregma, and to a depth of 7.2 mm below the duramater. 2 minutes after lowing the cannula, 2 μL of 6-OHDA is infused at a rate of 0.5 μL/min over 4 minutes, yeilding a final dose of 8 μg. The cannula is then left in place for a further 5 minutes to facilitate diffusion before being slowly withdrawn. The skin is then sutured shut using Ethicon W501 Mersilk, and the animal removed from the strereotaxic frame and returned to its homecage. The rats are allowed 2 weeks to recover from surgery before behavioural testing.

Apparatus

Rotational behaviour is measured using an eight station rotameter system provided by Med Associates, San Diego, USA. Each station is comprised of a stainless steel bowl (45 cm diameter x 15 cm high) enclosed in a transparent Plexiglas cover running around the edge of the bowl, and extending to a height of 29 cm. To assess rotation, rats are placed in cloth jacket attached to a spring tether connected to optical rotameter positioned above the bowl, which assesses movement to the left or right either as partial (45°) or full (360°) rotations. All eight stations are interfaced to a computer that tabulated data.

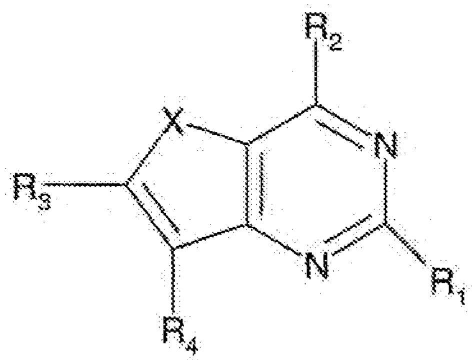
Procedure

To reduce stress during drug testing, rats are initially habituated to the apparatus for 15 minutes on four consecutive days. On the test day, rats are given an intraperitoneal injection of test compound 30 minutes prior to testing. Immediately prior to testing, animals are given a subcutaneous injection of a subthreshold dose of apomorphine, then placed in the harness and the number of rotations recorded for one hour. The total number of full

contralatral rotations during the hour test period serves as an index of antiparkinsonian drug efficacy.

CLAIMS

1. A compound of formula (I):



(I)

wherein

X is S or O;

R_1 is selected from H, alkyl, aryl, hydroxy, alkoxy, aryloxy, thioalkyl, thioaryl, halogen, CN, COR_5, CO_2R_5, $CONR_6R_7$, $CONR_5NR_6R_7$, NR_6R_7, $NR_5CONR_6R_7$, NR_5COR_6, $NR_5CO_2R_8$, and $NR_5SO_2R_8$;

R_2 is selected from aryl attached via an unsaturated carbon atom;

R_3 is selected from H, alkyl, hydroxy, alkoxy, halogen, CN and NO_2;

R_4 is selected from H, alkyl, aryl, hydroxy, alkoxy, aryloxy, thioalkyl, thioaryl, halogen, CN, NO_2, COR_5, CO_2R_5, $CONR_6R_7$, $CONR_5NR_6R_7$, NR_6R_7, $NR_5CONR_6R_7$, NR_5COR_6, $NR_5CO_2R_8$ and $NR_5SO_2R_8$;

R_5, R_6 and R_7 are independently selected from H, alkyl and aryl or where R_6 and R_7 are in an (NR_6R_7) group, R_6 and R_7 may be linked to form a heterocyclic group, or where R_5, R_6 and R_7 are in a ($CONR_5NR_6R_7$) group, R_5 and R_6 may be linked to form a heterocyclic group; and

R_8 is selected from alkyl and aryl,

or a pharmaceutically acceptable salt thereof or prodrug thereof.

2. A compound according to claim 1 wherein X is S.

3. A compound according to claim 1 or 2 wherein R_1 is selected from alkyl, alkoxy, thioalkyl, NR_6R_7 and NR_5COR_6.

4. A compound according to claim 1 or 2 wherein R_1 is selected from alkyl and NR_6R_7.

5. A compound according to claim 1, 2, 3 or 4 wherein R_1 is selected from haloalkyl and arylalkyl.

6. A compound according to any preceding claim wherein R_2 is a 5- or 6 membered monocyclic aryl group.

7. A compound according to any preceding claim wherein R_2 is a heteroaryl group.

8. A compound according to claim 7 wherein R_2 is a heteroaryl group which is attached to the pyrimidine ring of formula (I) such that a heteroatom is adjacent to the unsaturated carbon atom attached to said pyrimidine ring.

9. A compound according to claim 7 or 8 wherein R_2 is an N, O or S-containing heteroaryl group.

10. A compound according to any preceding claim wherein R_2 is not ortho,ortho-disubstituted.

11. A compound according to any preceding claim wherein R_2 is not ortho-substituted.

12. A compound according to any preceding claim wherein R_2 is selected from furyl, thienyl, pyridyl and thiazolyl.

13. A compound according to any preceding claim wherein R_2 is selected from 2-furyl, 2-thienyl, 2-thiazolyl and 2-pyridyl.

14. A compound according to any preceding claim wherein R_3 is selected from H, CF_3, hydroxy, alkoxy, halogen, CN and NO_2.

15. A compound according to any preceding claim wherein R_3 is H.

16. A compound according to claim 1 wherein R_3 is selected from alkyl or alkoxy and said alkyl group or the alkyl group of said alkoxy is selected from C_{1-6} alkyl.

17. A compound according to any preceding claim wherein R_4 is selected from H, alkyl, halogen, COR_5, CO_2R_5, $CONR_6R_7$ and $CONR_5NR_6R_7$.

18. A compound according to any preceding claim wherein R_4 is selected from H, alkyl and halogen

19. A compound according to claim 18 wherein R_4 is selected from C_{1-6} alkyl.

20. A compound according to claim 18 or 19 wherein R_4 is selected from haloalkyl and arylalkyl.

21. A compound according to any of claims 1 to 18 wherein R_4 is H.

22. A compound according to any of claims 1 to 21 wherein R_6 and R_7 are linked to form a saturated heterocyclic ring.

23. A compound according to any of claims 1 to 22 wherein R_6 and R_7 are linked to form a 5 or 6-membered heterocyclic ring.

24. A compound according to any of claims 1 to 21 wherein R_5 to R_8 are independently selected from C_{1-6} alkyl.

25. A compound according to any of claims 1 to 21 wherein R_5 to R_7 are independently selected from H.

26. A compound according to claim 1 which is selected from:

7-bromo-4-(2-furyl)-N-(2-hydroxyethyl)thieno[3,2-d]pyrimidine-2-amine;
N-allyl-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine;
2-ethyl-4-(2-pyridyl)thieno[3,2-d]pyrimidine;
2-methyl-4-(2-pyridyl)thieno[3,2-d]pyrimidine;
2-*n*-propyl-4-(2-pyridyl)thieno[3,2-d]pyrimidine;
N-(2-hydroxyethyl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine;
2-isopropyl-4-(2-pyridyl)thieno[3,2-d]pyrimidine;
N-(2-methoxyethyl)-4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine;
N,N-dimethyl-4-(4-methyl-2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine;
4-(2-furyl)thieno[3,2-d]pyrimidine-2-amine;
2-ethyl-4-(4-methyl-2-thiazolyl)thieno[3,2-d]pyrimidine;
2-ethyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine;
N,N-dimethyl-4-(5-methyl-2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine;
N,N-dimethyl-4-(4,5-dimethyl-2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine;
4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine;
(2R)-2-(2-hydroxymethylpyrrolidin-1-yl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine;
N-allyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine-2-amine;
2-isopropyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine;
N,N-dimethyl-4-(5-methyl-2-pyridyl)thieno[3,2-d]pyrimidine-2-amine;
2-*tert*-butyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine;
2-cyclopropyl-4-(2-thiazolyl)thieno[3,2-d]pyrimidine;
2-ethyl-4-(6-methyl-2-pyridyl)thieno[3,2-d]pyrimidine;
(2S)-2-(2-hydroxymethylpyrrolidin-1-yl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine; and
2-(2-chloroethyl)-4-(2-thiazolyl)thieno[3,2-d]pyrimidine.

27. A compound according to any one of claims 1 to 26, or a pharmaceutically acceptable salt thereof, for use in therapy.

28. The use of a compound according to any of claims 1 to 26 or a pharmaceutically acceptably salt thereof in the manufacture of a medicament for the treatment or prevention of a disorder in which the blocking of purine receptors may be beneficial.

29. A method of treating or preventing a disorder in which the blocking of purine receptors may be beneficial comprising administration to a subject in need of such treatment an effective dose of a compound as set out in any one of claims 1 to 26 or a pharmaceutically acceptable salt thereof.

30. A use or method according to claim 28 or 29 wherein the disorder is caused by the hyperfunctioning of purine receptors.

31. A use or method according to any one of claims 28 to 30 wherein the purine receptors are adenosine receptors.

32. A use or method according to claim 31 wherein the adenosine receptors are A_{2A} receptors.

33. Use of a compound as set out in any one of claims 1 to 26 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment or prevention of movement disorders in a subject.

34. A method of treating or preventing movement disorders comprising administration to a subject in need of such treatment an effective dose of a compound as set out in any one of claims 1 to 26 or a pharmaceutically acceptable salt thereof.

35. A use or method according to claim 33 or 34 wherein the movement disorder is Parkinson's disease.

36. A use or method according to claim 35 for treatment of drug-induced Parkinsonism, post-encephalitic Parkinsonism, Parkinsonism induced by poisoning or post-traumatic Parkinson's disease.

37. A use or method according to claim 33 or 34 wherein the movement disorder is progressive supernuclear palsy, Huntingtons disease, multiple system atrophy, corticobasal degeneration, Wilsons disease, Hallerrorden-Spatz disease, progressive pallidal atrophy, Dopa-responsive dystonia-Parkinsonism, spasticity or other disorders of the basal ganglia which result in dyskinesias.

38. A use or method according to any one of claims 33 to 37 wherein the compound of formula (I) is in combination with one or more additional drugs useful in the treatment of movement disorders, the components being in the same formulation or in separate formulations for administration simultaneously or sequentially.

39. A use or method according to claim 38 wherein said additional drug(s) useful in the treatment of movement disorders is/are a drug useful in the treatment of Parkinson's disease.

40. A use or method according to claim 38 or 39 wherein the or one of the additional drugs is L-DOPA or a dopamine agonist.

41. A use or method according to any one of claims 28 to 32 wherein said disorder is depression, cognitive or memory impairment, acute or chronic pain, ADHD or narcolepsy.

42. A use or method according to any one of claims 28 to 32 wherein said cognitive or memory impairment disorder is Alzheimer's disease.

43. Use of a compound as set out in any one of claims 1 to 26 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for neuroprotection in a subject.

44. A method of neuroprotection comprising administration to a subject in need of such treatment an effective dose of a compound as set out in any one of claims 1 to 26 or a pharmaceutically acceptable salt thereof.

45. A use or method according to claim 43 or 44 wherein said medicament or said method is for neuroprotection in a subject suffering from or at risk from a neurodegenerative disorder.

46. A use or method according to claim 45 wherein said neurodegenerative disorder is a movement disorder.

47. A use or method according to claim 46 wherein said movement disorder is a disorder as set out in claim 35, 36 or 37.

48. A use or method according to any one of claims 28 to 47 wherein the subject is human.

INTERNATIONAL SEARCH REPORT

PCT/GB 02/00084

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D495/04 A61K31/505 A61P25/28 //(C07D495/04,333:00, 239:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data, BIOSIS, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PATENT ABSTRACTS OF JAPAN vol. 016, no. 207 (C-0941), 18 May 1992 (1992-05-18) -& JP 04 036284 A (SUMITOMO CHEM CO LTD), 6 February 1992 (1992-02-06) abstract	1,6,10, 11, 16-18,21
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
25 April 2002	07/05/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Steendijk, M

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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